```
=> d his nofile

     (FILE 'HOME' ENTERED AT 13:28:46 ON 11 MAY 2006)

     FILE 'REGISTRY' ENTERED AT 13:28:52 ON 11 MAY 2006
L1              STRUCTURE UPLOADED
L2              QUE ABB=ON  PLU=ON  L1
                D L1
L3            0 SEA SSS SAM L1

     FILE 'STNGUIDE' ENTERED AT 13:56:24 ON 11 MAY 2006

     FILE 'CAPLUS' ENTERED AT 14:11:12 ON 11 MAY 2006
                E US2003-646904/APPS
L4            1 SEA ABB=ON  PLU=ON  US2003-646904/AP
                SEL RN L4

     FILE 'REGISTRY' ENTERED AT 14:11:34 ON 11 MAY 2006
L5           18 SEA ABB=ON  PLU=ON  (114977-28-5/BI OR 15663-27-1/BI OR
                158181-47-6/BI OR 158181-54-5/BI OR 158181-56-7/BI OR 180288-69
                -1/BI OR 184475-35-2/BI OR 220127-57-1/BI OR 23214-92-8/BI OR
                33069-62-4/BI OR 3778-73-2/BI OR 41575-94-4/BI OR 50-18-0/BI
                OR 51-21-8/BI OR 53643-48-4/BI OR 57-22-7/BI OR 59-05-2/BI OR
                674799-35-0/BI)
L6            1 SEA ABB=ON  PLU=ON  C43 H54 N2 O11/MF AND L5
                D RSD
L7            7 SEA ABB=ON  PLU=ON  NC2OC11NC2OC11/ES
L8           51 SEA ABB=ON  PLU=ON  NC2OC11NC2OC11/ESS
                D SCAN L7
L9           44 SEA ABB=ON  PLU=ON  L8 NOT L7
L10      387155 SEA ABB=ON  PLU=ON  NCOC2/ESS
L11          37 SEA ABB=ON  PLU=ON  L10 AND L9

     FILE 'CAPLUS' ENTERED AT 14:26:23 ON 11 MAY 2006
L12          15 SEA ABB=ON  PLU=ON  L11

     FILE 'BEILSTEIN' ENTERED AT 14:27:19 ON 11 MAY 2006
L13             STRUCTURE UPLOADED
L14             QUE ABB=ON  PLU=ON  L13
L15          30 SEA SSS FUL L13
L16          30 SEA ABB=ON  PLU=ON  L15 NOT L8
                D QUE

     FILE 'STNGUIDE' ENTERED AT 14:29:57 ON 11 MAY 2006

     FILE 'BEILSTEIN' ENTERED AT 14:33:43 ON 11 MAY 2006
L17             STRUCTURE UPLOADED
L18             QUE ABB=ON  PLU=ON  L17
L19          29 SEA SSS FUL L17

     FILE 'STNGUIDE' ENTERED AT 14:35:53 ON 11 MAY 2006

     FILE 'BEILSTEIN' ENTERED AT 14:48:13 ON 11 MAY 2006
L20             STRUCTURE UPLOADED
L21             QUE ABB=ON  PLU=ON  L20
L22          24 SEA SSS FUL L20
L23             STRUCTURE UPLOADED
L24             QUE ABB=ON  PLU=ON  L23
L25          24 SEA SSS FUL L23
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                D IDE ALLREF 1

     FILE 'CAPLUS' ENTERED AT 14:54:51 ON 11 MAY 2006
L26             0 SEA ABB=ON  PLU=ON  L12 AND WIPF/AU
L27             2 SEA ABB=ON  PLU=ON  L12 AND WIPF?/AU
                D BIB 1-2
L28             6 SEA ABB=ON  PLU=ON  L12 NOT (PY>2002 OR AY>2002 OR PRY>2002)
                E IRSCHIK H/AU
L29            88 SEA ABB=ON  PLU=ON  ("IRSCHIK H"/AU OR "IRSCHIK HERBERT"/AU OR
                "IRSCHIK HERBERT DIPL BIOL"/AU OR "IRSCHIK HERBET"/AU)
                E JANSEN R/AU
L30           225 SEA ABB=ON  PLU=ON  ("JANSEN R"/AU OR "JANSEN R A"/AU OR
                "JANSEN R C"/AU OR "JANSEN R E"/AU OR "JANSEN R F"/AU OR
                "JANSEN R H"/AU OR "JANSEN R H J"/AU OR "JANSEN R H S"/AU OR
                "JANSEN R J"/AU OR "JANSEN R J E"/AU OR "JANSEN R J J"/AU OR
                "JANSEN R K"/AU OR "JANSEN R L H"/AU OR "JANSEN R M W"/AU OR
                "JANSEN R P"/AU OR "JANSEN R P M"/AU OR "JANSEN R P S"/AU OR
                "JANSEN R T P"/AU OR "JANSEN R W"/AU OR "JANSEN R W M"/AU OR
                "JANSEN R W M M"/AU OR "JANSEN RALF"/AU OR "JANSEN RALF P"/AU
                OR "JANSEN RALF PETER"/AU OR "JANSEN RALPH"/AU)
                E SASSE F/AU
L31            72 SEA ABB=ON  PLU=ON  ("SASSE F"/AU OR "SASSE F J"/AU OR "SASSE
                FLORENZ"/AU)
                E BAASNER S/AU
L32            22 SEA ABB=ON  PLU=ON  ("BAASNER S"/AU OR "BAASNER SIIKE"/AU OR
                "BAASNER SILKE"/AU)
                E GUNTER E/AU
L33            14 SEA ABB=ON  PLU=ON  ("GUNTER E"/AU OR "GUNTER E J"/AU OR
                "GUNTER E N"/AU OR "GUNTER E W"/AU OR "GUNTER ECKHARD"/AU)
L34             2 SEA ABB=ON  PLU=ON  (L29 OR L30 OR L31 OR L32 OR L33) AND L28
L35            13 SEA ABB=ON  PLU=ON  (L29 AND (L30 OR L31 OR L32 OR L33)) OR
                (L30 AND (L31 OR L32 OR L33)) OR (L31 AND (L32 OR L33)) OR
                (L32 AND L33)
L36            21 SEA ABB=ON  PLU=ON  DISORAZOL?/OBI
L37            88 SEA ABB=ON  PLU=ON  ONCOS?/OBI (L) (BENIGH/OBI OR MALIGN?/OBI
                OR CANCER?/OBI)
L38             6 SEA ABB=ON  PLU=ON  (L36 OR L37) AND (L29 OR L30 OR L31 OR L32
                OR L33)
L39             5 SEA ABB=ON  PLU=ON  L38 NOT L35
L40          7815 SEA ABB=ON  PLU=ON  BENIGN?/OBI
L41             3 SEA ABB=ON  PLU=ON  L40 AND (L29 OR L30 OR L31 OR L32 OR L33)
L42             8 SEA ABB=ON  PLU=ON  (L39 OR L41)
L43            18 SEA ABB=ON  PLU=ON  (L42 OR L12)
L44            15 SEA ABB=ON  PLU=ON  L43 NOT L41
                D QUE L12

=> d que l12
L7              7 SEA FILE=REGISTRY ABB=ON  PLU=ON  NC2OC11NC2OC11/ES
L8             51 SEA FILE=REGISTRY ABB=ON  PLU=ON  NC2OC11NC2OC11/ESS
L9             44 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 NOT L7
L10        387155 SEA FILE=REGISTRY ABB=ON  PLU=ON  NCOC2/ESS
L11            37 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND L9
L12            15 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11


=> d ibib abs hitstr l12 tot

L12  ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:140060  CAPLUS
```
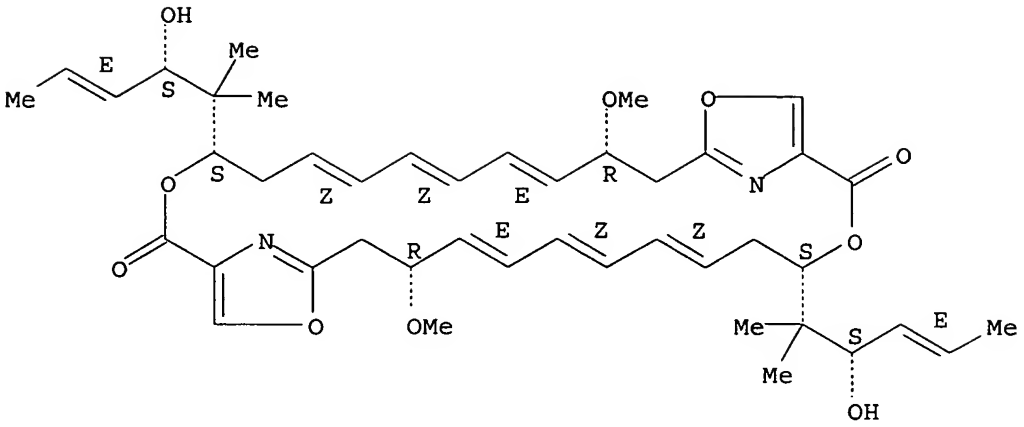

DOCUMENT NUMBER: 144:246545
TITLE: Cellular analysis of disorazole C1 and structure-activity relationship of analogs of the natural product
AUTHOR(S): Wipf, Peter; Graham, Thomas H.; Vogt, Andreas; Sikorski, Rachel P.; Ducruet, Alexander P.; Lazo, John S.
CORPORATE SOURCE: Department of Chemistry, Center for Chemical Methodologies and Library Development, University of Pittsburgh Drug Discovery Institute, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SOURCE: Chemical Biology & Drug Design (2006), 67(1), 66-73
CODEN: CBDDAL; ISSN: 1747-0277
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Structure-activity analyses of synthetic disorazole C1 and eight of its analogs indicate that the presence of a vinyl oxirane moiety or a tetraene sequence is not necessary for potent cytotoxic and antimitotic properties. Using an automated multiparameter fluorescence-based cellular assay to simultaneously probe the effects of disorazole analogs on cellular microtubules, mitotic arrest, and cytotoxicity, we found that disorazole C1 enhanced the mitotic index and chromatin condensation and arrested cells in the G2/M phase of the cell cycle. All structural analogs and synthesis precursors of disorazole C1 were at least two orders of magnitude less potent than the parent compound, thus indicating that both the functional group array and the three-dimensional conformation of the parent compound are critical for interaction with the biol. target. We conclude that disorazole C1 is a potent inducer of mitotic arrest and hypothesize that this biol. activity may be mediated by microtubule perturbation.
IT **158181-52-3**, Disorazole C1 **809285-62-9**
809285-88-9 877475-91-7
RL: PAC (Pharmacological activity); BIOL (Biological study)
(cellular anal. of disorazole C1 and structure-activity relationship of analogs of the natural product)
RN 158181-52-3 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,24,26,30(33),32-decaene-2,18-dione, 4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-, (4S,6Z,8Z,10E,12R,20S,22Z,24Z,26E,28R)- (9CI) (CA INDEX NAME)

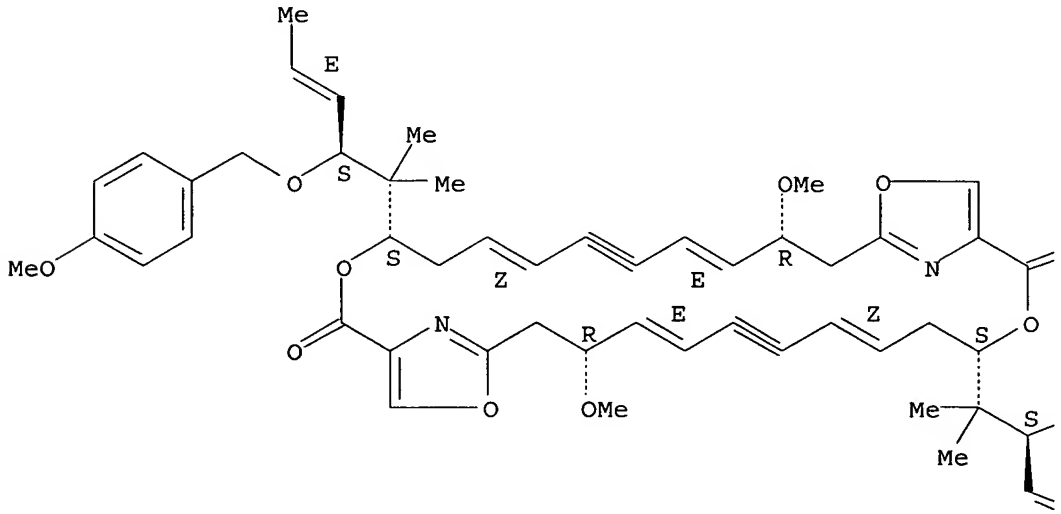
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



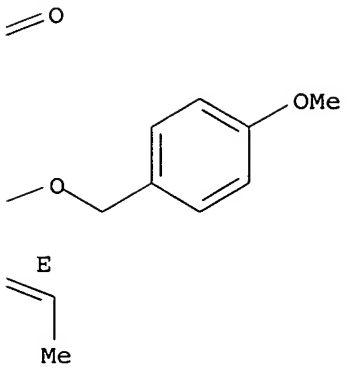
RN 809285-62-9 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,10,14(34),16,22,26,30(33),32-octaene-8,24-diyne-2,18-dione, 12,28-dimethoxy-4,20-bis[(2S,3E)-2-[(4-methoxyphenyl)methoxy]-1,1-dimethyl-3-pentenyl]-, (4S,6Z,10E,12R,20S,22Z,26E,28R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as described by E or Z.

PAGE 1-A

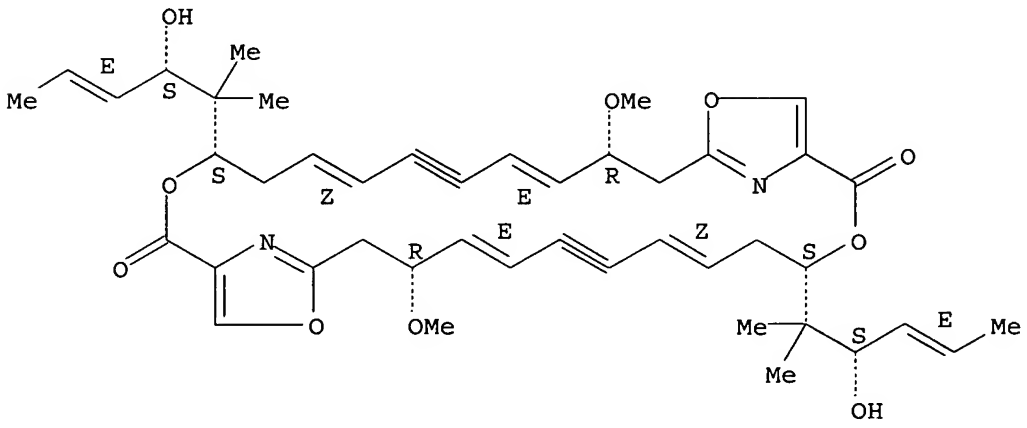


PAGE 1-B



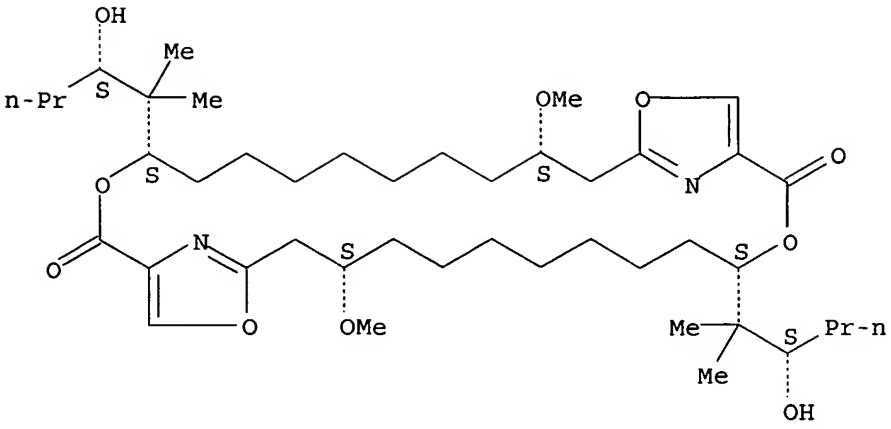
RN 809285-88-9 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,10,14(34),16,22,26,30(33),32-octaene-8,24-diyne-2,18-dione, 4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-, (4S,6Z,10E,12R,20S,22Z,26E,28R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as described by E or Z.



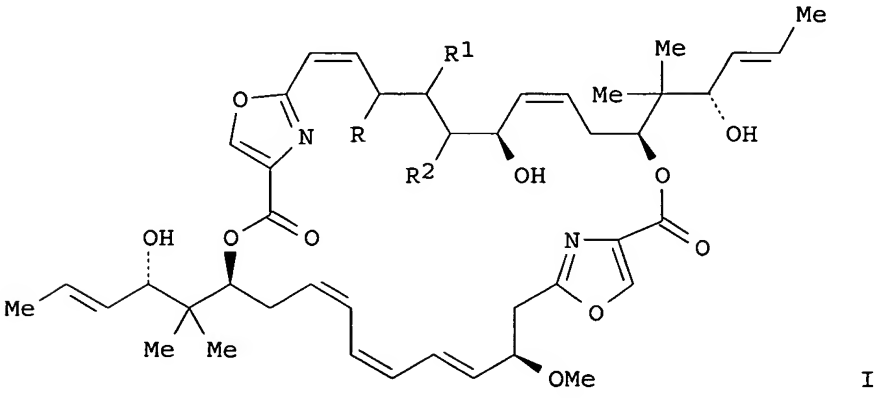
RN 877475-91-7 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-14(34),16,30(33),32-tetraene-2,18-dione, 4,20-bis[(2S)-2-hydroxy-1,1-dimethylpentyl]-12,28-dimethoxy-, (4S,12S,20S,28S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1302742 CAPLUS
DOCUMENT NUMBER: 144:192008
TITLE: Methanolysis Products of Disorazole A1
AUTHOR(S): Hearn, Brian R.; Arslanian, Robert L.; Fu, Hong; Liu, Fenghua; Gramajo, Hugo; Myles, David C.
CORPORATE SOURCE: Kosan Biosciences, Inc., Hayward, CA, 94545, USA
SOURCE: Journal of Natural Products (2006), 69(1), 148-150
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Chemical Society-American Society of Pharmacognosy
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Two new disorazole analogs were synthesized by acid-promoted methanolysis of disorazole A1. Structural elucidation of both products I (RR1 = bond, R2 = MeO; R = MeO, R1R2 = bond), through 1D and 2D NMR expts., verified that each resulted from epoxide cleavage. With antiproliferative activities in susceptible cell lines comparable to that of disorazole A1, these methanolysis products indicate that the C-9-C-10 epoxide is not an

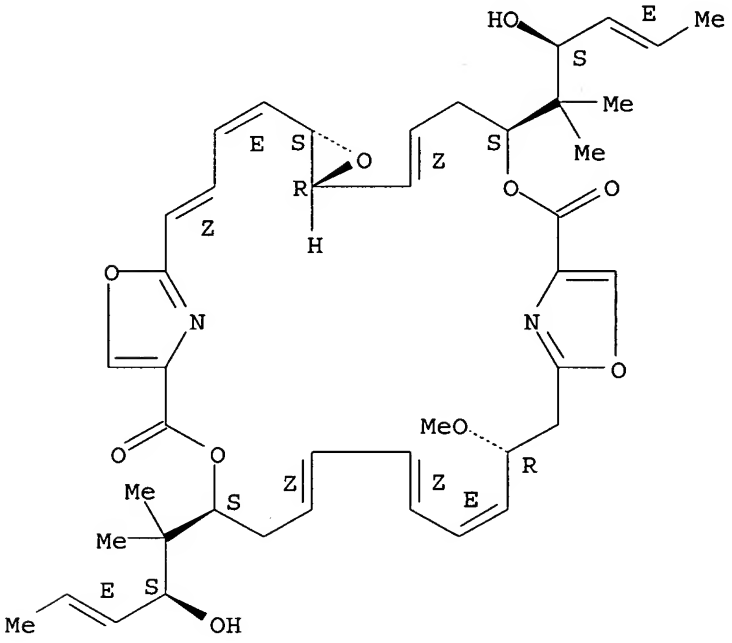
essential structural component for biol. activity.

IT **158181-47-6**
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(methanolysis of disorazole A1, antitumor activity, and structure-activity relationship)

RN 158181-47-6 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



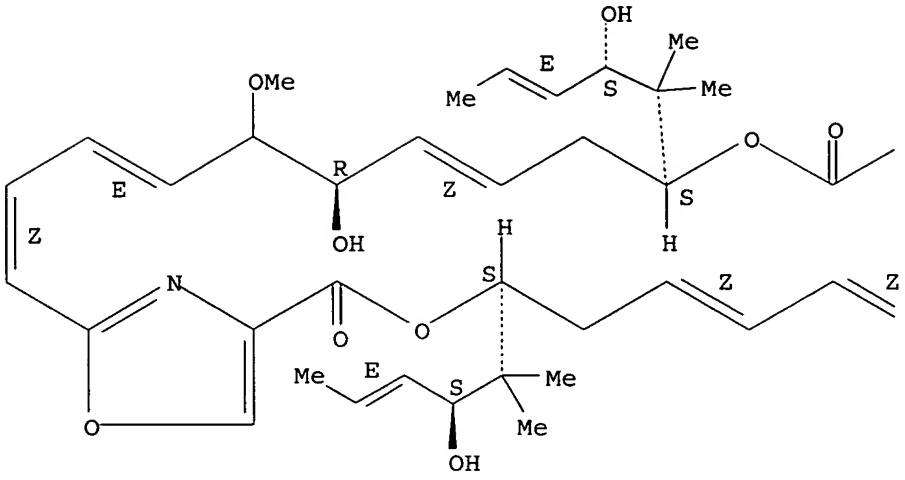
IT **875292-06-1P 875292-07-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(methanolysis of disorazole A1, antitumor activity, and structure-activity relationship)

RN 875292-06-1 CAPLUS

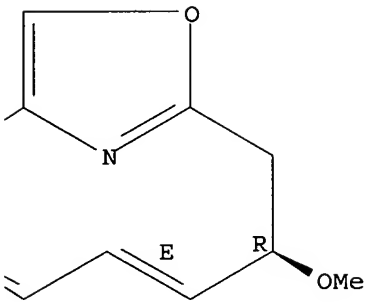
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,26,28,30(33),32-decaene-2,18-dione, 24-hydroxy-4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,25-dimethoxy-, (4S,6Z,8Z,10E,12R,20S,22Z,24R,26E,28Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



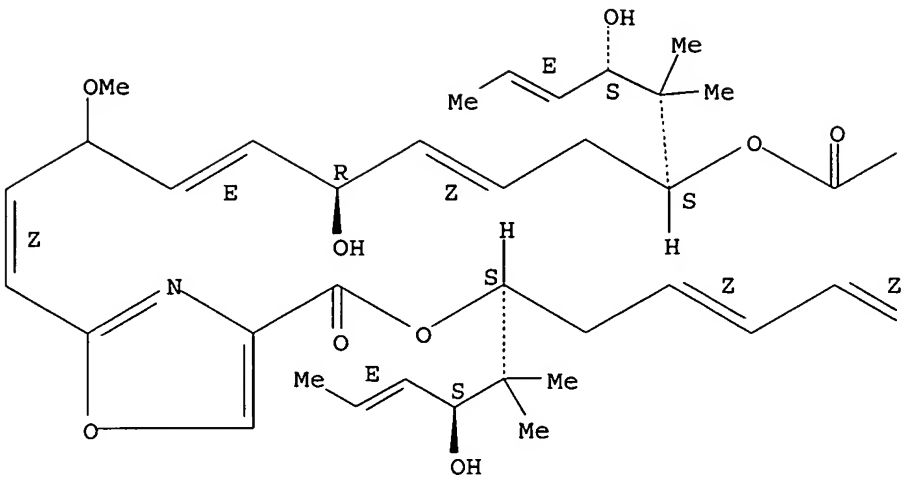
PAGE 1-B



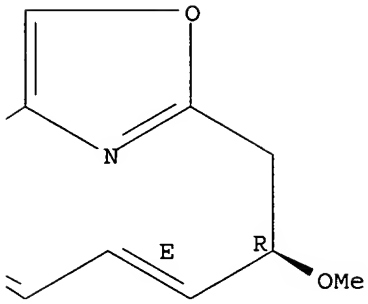
RN 875292-07-2 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,25,28,30(33),32-decaene-2,18-dione, 24-hydroxy-4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,27-dimethoxy-, (4S,6Z,8Z,10E,12R,20S,22Z,24R,25E,28Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1024991 CAPLUS
DOCUMENT NUMBER: 144:1150
TITLE: The biosynthetic genes for disorazoles, potent cytotoxic compounds that disrupt microtubule formation
AUTHOR(S): Carvalho, Ruby; Reid, Ralph; Viswanathan, Nina; Gramajo, Hugo; Julien, Bryan
CORPORATE SOURCE: Kosan Biosciences, Inc., Hayward, CA, 94545, USA
SOURCE: Gene (2005), 359, 91-98
CODEN: GENED6; ISSN: 0378-1119
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Disorazoles are polyketides produced by the myxobacterium Sorangium cellulosum So ce12. Their mode of action is to inhibit tubulin polymerization and destabilize microtubules. Using transposon mutagenesis, two mutant strains were identified that produced no disorazoles. Sequencing the DNA flanking the insertions revealed a polyketide synthase gene cluster that

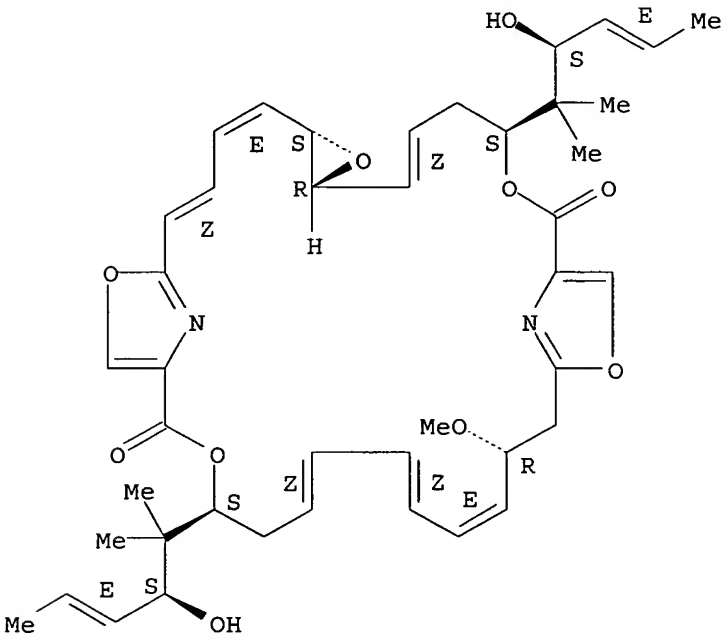
would encode three polypeptides, DszA, DszB, and DszC, with DszC containing both nonribosomal peptide synthetase and polyketide synthase modules. The disorazole polyketide synthase modules lack an acyltransferase domain. Instead, a sep. gene, dszD, encodes an AT protein, thus revealing that the disorazole gene cluster falls into the trans-AT Type I family of PKS enzymes.

IT **158181-47-6**, Disorazole A1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biosynthetic genes for disorazoles, potent cytotoxic compds. that disrupt microtubule formation)

RN 158181-47-6 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:669790 CAPLUS
DOCUMENT NUMBER: 143:455774
TITLE: Production of the tubulin destabilizer disorazol in Sorangium cellulosum: Biosynthetic machinery and regulatory genes
AUTHOR(S): Kopp, Maren; Irschik, Herbert; Pradella, Silke; Mueller, Rolf
CORPORATE SOURCE: Pharmaceutical Biotechnology, Saarland University, Saarbruecken, 66123, Germany

SOURCE: ChemBioChem (2005), 6(7), 1277-1286
CODEN: CBCHFX; ISSN: 1439-4227
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

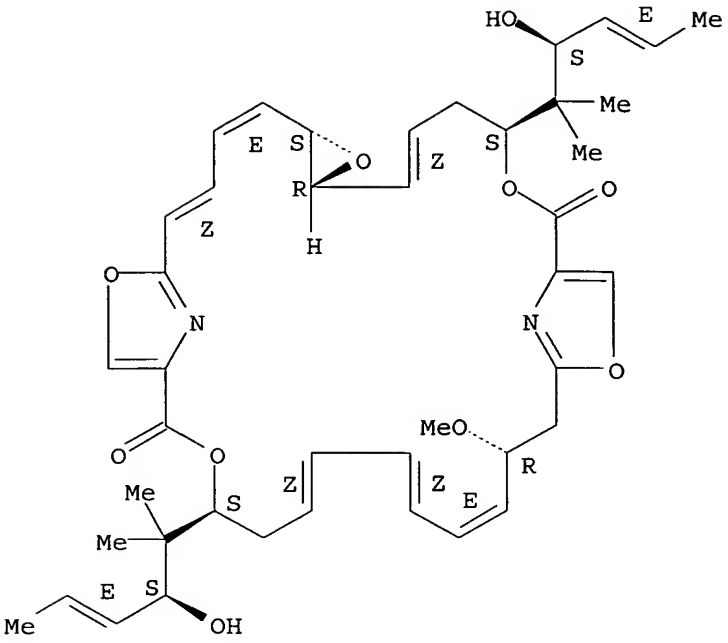
AB Myxobacteria show a high potential for the production of natural compds. that exhibit a wide variety of antibiotic, antifungal, and cytotoxic activities. The genus Sorangium is of special biotechnol. interest because it produces almost half of the secondary metabolites isolated from these microorganisms. We describe a transposon-mutagenesis approach to identifying the disorazol biosynthetic gene cluster in Sorangium cellulosum So ce12, a producer of multiple natural products. In addition to the highly effective disorazol-type tubulin destabilizers, S. cellulosum So ce12 produces sorangicins, potent eubacterial RNA polymerase inhibitors, bactericidal sorangiolides, and the antifungal chivosazoles. To obtain a transposon library of sufficient size suitable for the identification of the presumed biosynthetic gene clusters, an efficient transformation method was developed. We present here the first electroporation protocol for a strain of the genus Sorangium. The transposon library was screened for disorazol-neg. mutants. This approach led to the identification of the corresponding trans-acyltransferase core biosynthetic gene cluster together with a region in the chromosome that is likely to be involved in disorazol biosynthesis. A third region in the genome harbors another gene that is presumed to be involved in the regulation of disorazol production A detailed anal. of the biosynthetic and regulatory genes is presented in this paper.

IT **158181-47-6**, Disorazole A1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(genes involved in biosynthesis of disorazol A1 in Sorangium cellulosum)

RN 158181-47-6 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

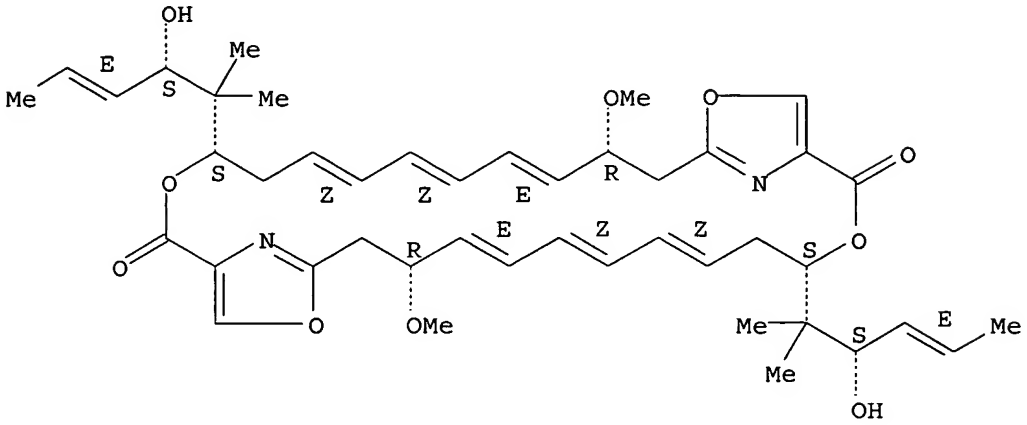


REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:930309 CAPLUS
DOCUMENT NUMBER: 142:74380
TITLE: Total Synthesis of (-)-Disorazole C1
AUTHOR(S): Wipf, Peter; Graham, Thomas H.
CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SOURCE: Journal of the American Chemical Society (2004), 126(47), 15346-15347
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:74380
GI

(4S,6Z,8Z,10E,12R,20S,22Z,24Z,26E,28R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

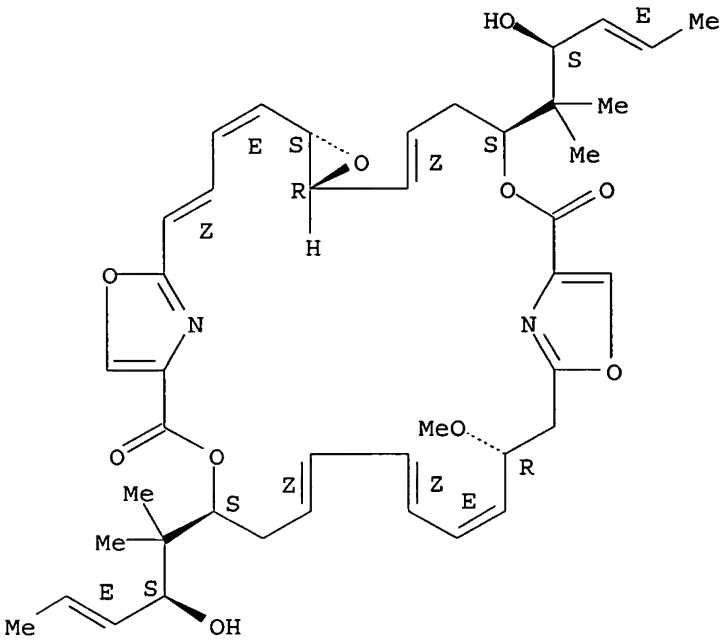
L12 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:366741 CAPLUS
DOCUMENT NUMBER: 137:169363
TITLE: Structural and stereochemical diversity from (±)-2,2-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one - application to the synthesis of polyketide segments of natural products
AUTHOR(S): Vakalopoulos, Alexandros; Smits, Rene; Hoffmann, H. Martin R.
CORPORATE SOURCE: Pharma Research, Bayer AG, Wuppertal, 42096, Germany
SOURCE: European Journal of Organic Chemistry (2002), (9), 1538-1545
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:169363

AB The racemic title compound was transformed into both cyclic and acyclic segments of bioactive natural products, including the C10-C17 segment of pederin, the C12-C19 (C12'-C19') segment of disorazole and the C1-C9 segment of auriside. A methodol. for the opening of six-membered ring acetals, containing gem-di-Me groups, to δ-hydroxy-1,3-dithianes was developed.

IT **158181-47-6P**, Disorazole A1
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of polyketide segments of pederin, disorazole and auriside from (±)-2,2-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one involving the development of ring opening methodol. for six-membered ring acetals to δ-hydroxy-1,3-dithianes)

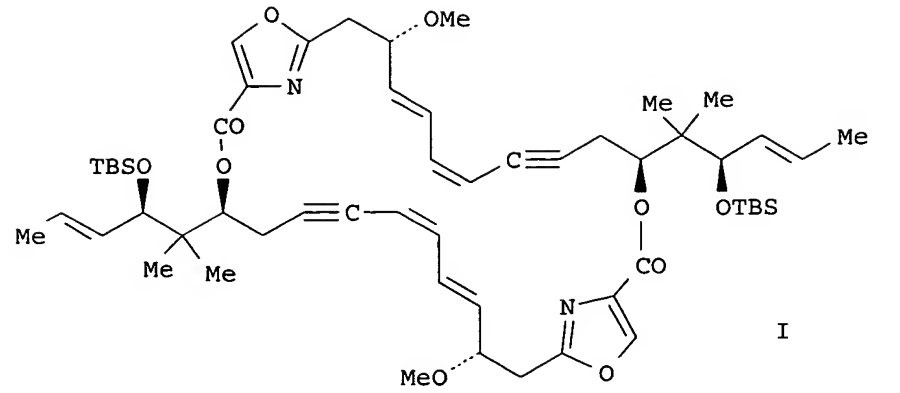
RN 158181-47-6 CAPLUS
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

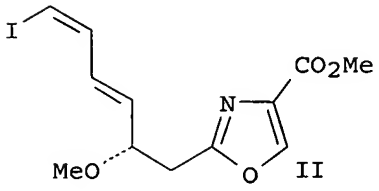


REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

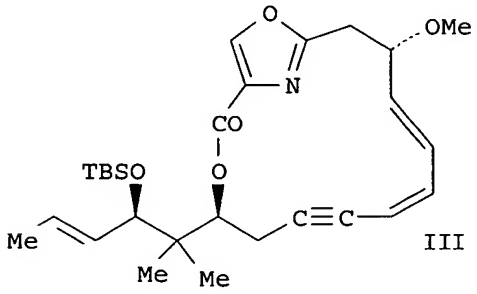
L12 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:569995 CAPLUS
DOCUMENT NUMBER: 135:331280
TITLE: Studies on the Total Synthesis of Disorazole C1. An Advanced Macrocycle Intermediate
AUTHOR(S): Hillier, M. C.; Price, A. T.; Meyers, A. I.
CORPORATE SOURCE: Department of Chemistry, Colorado State University, Fort Collins, CO, 80523, USA
SOURCE: Journal of Organic Chemistry (2001), 66(18), 6037-6045
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:331280
GI



I



II



III

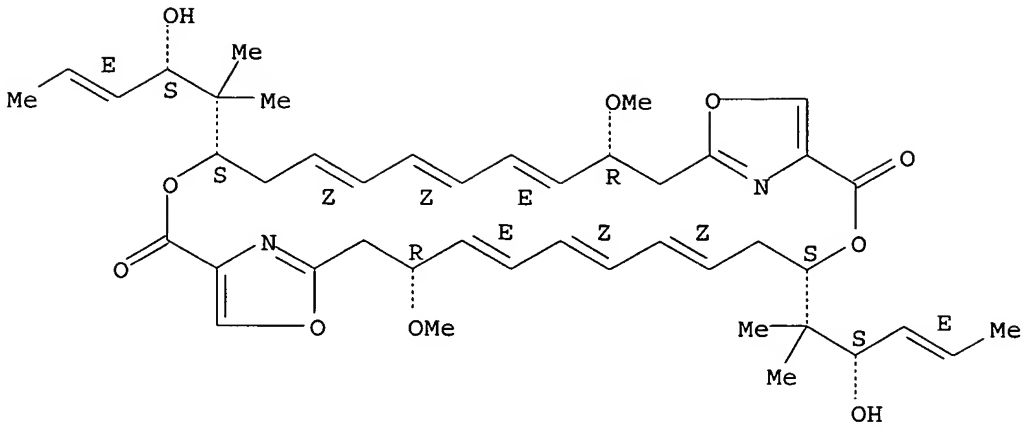
AB Synthesis of protected tetradehydro-(6,6'-S)-(14,14'-S)-(16,16'-R)-disorazole (I), a potential precursor to the natural product disorazole C1, is described. Key features of this work include (a) an unprecedented sequential 1,5 O→O silyl rearrangement/Horner-Wadsworth-Emmons reaction used to construct (R,E,E)-MeCH=CHCH(OCMe3)CMe2CH=CHCO2Et, (b) a highly convergent Sonogashira reaction between the dienyl iodide (II) and the alkyne (R,S,E)-MeCH=CHCH(OSiMe2CMe3)CMe2CH(OH)CH2C.tplbond.CH to assemble the dienyne monomeric fragment, and (c) the selective cyclization to give either the cyclic monomer (III) or the dimer I.

IT **158181-52-3P**, Disorazole C1
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of an advanced macrocyclic intermediate of disorazole C1)

RN 158181-52-3 CAPLUS

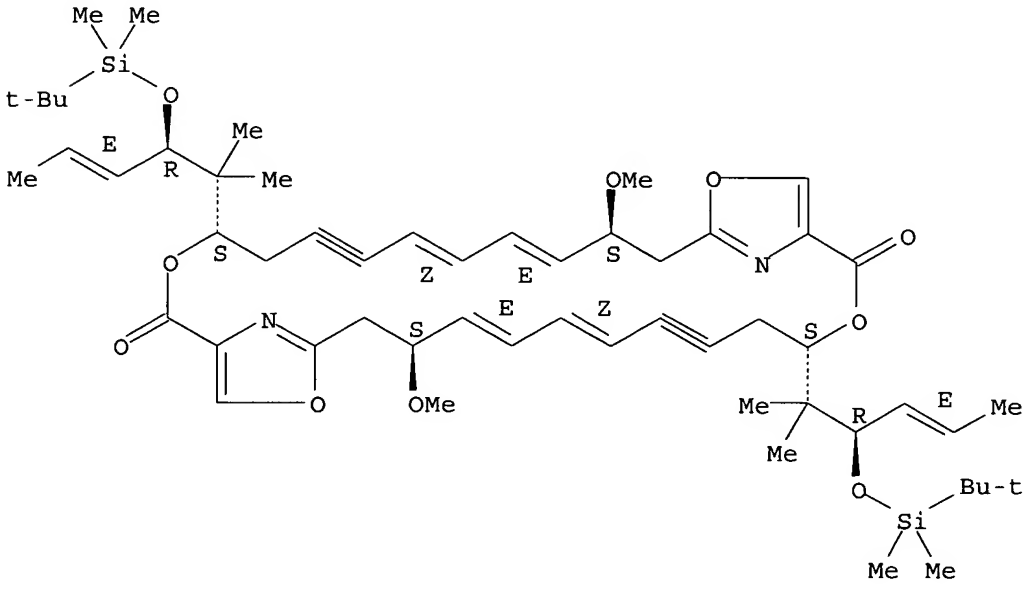
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,24,26,30(33),32-decaene-2,18-dione, 4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-, (4S,6Z,8Z,10E,12R,20S,22Z,24Z,26E,28R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



IT **365217-54-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of an advanced macrocyclic intermediate of disorazole C1)
RN 365217-54-5 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-8,10,14(34),16,24,26,30(33),32-octaene-6,22-diyne-2,18-dione, 4,20-bis[(2R,3E)-2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-, (4S,8Z,10E,12S,20S,24Z,26E,28S)- (9CI) (CA INDEX NAME)

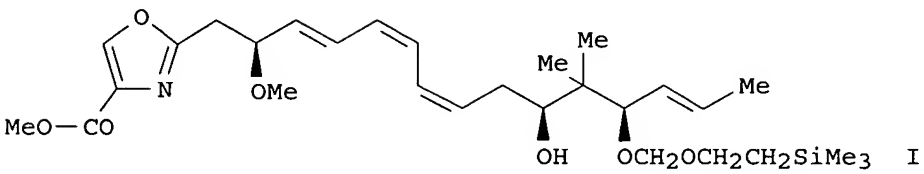
Absolute stereochemistry. Rotation (+).
Double bond geometry as described by E or Z.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:303505 CAPLUS
DOCUMENT NUMBER: 133:58648
TITLE: The synthesis of the monomeric moiety of disorazole C1
AUTHOR(S): Hillier, M. C.; Park, D. H.; Price, A. T.; Ng, R.; Meyers, A. I.
CORPORATE SOURCE: Department of Chemistry, Colorado State University, Fort Collins, CO, 80523, USA
SOURCE: Tetrahedron Letters (2000), 41(16), 2821-2824
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:58648
GI



I

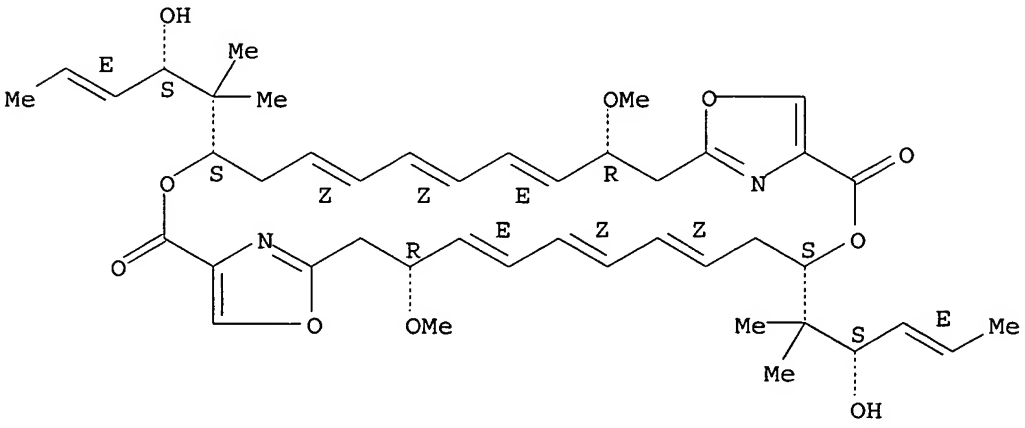
AB The stereocontrolled synthesis of the monomeric subunit (I) of the macrolide dimer disorazole C1 has been accomplished by convergent coupling using the Stille method.

IT **158181-52-3P**, Disorazole C1
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of monomeric moiety of disorazole C1)

RN 158181-52-3 CAPLUS

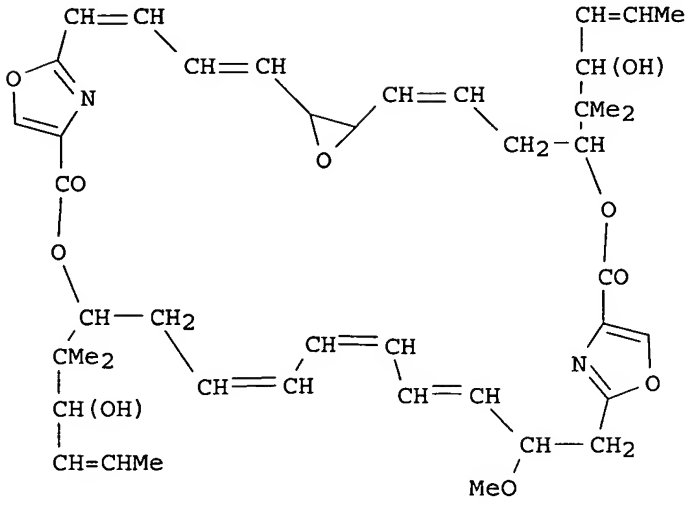
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,24,26,30(33),32-decaene-2,18-dione, 4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-, (4S,6Z,8Z,10E,12R,20S,22Z,24Z,26E,28R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:333405 CAPLUS
DOCUMENT NUMBER: 122:128225
TITLE: Disorazol A, an efficient inhibitor of eukaryotic organisms isolated from myxobacteria
AUTHOR(S): Irschik, Herbert; Jansen, Rolf; Gerth, Klaus; Hoefle, Gerhard; Reichenbach, Hans
CORPORATE SOURCE: Dep. Biology Natural Products, Gesellschaft fuer Biotechnologische Forschung, Braunschweig, D-38124, Germany
SOURCE: Journal of Antibiotics (1995), 48(1), 31-5
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A new antibiotic, disorazol (I), was isolated from the culture broth of the myxobacterium Sorangium cellulosum strain So ce 12. It is a macrocyclic compound containing two oxazole rings. The antibiotic acted against many fungi and mammalian cell cultures. The latter responded to extremely low doses (MIC 3-30 pg/mL). None of the tested bacteria and yeasts were inhibited.

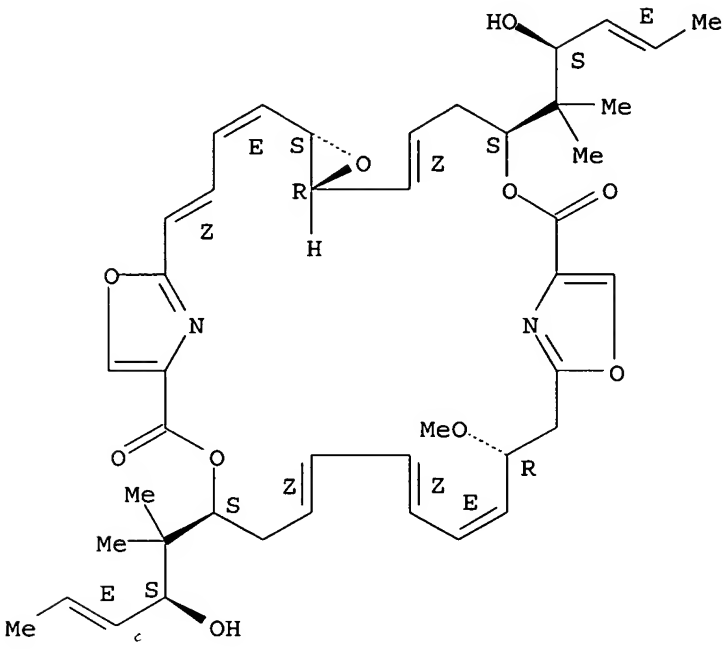
IT **158181-47-6P**, Disorazol A
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(disorazol A as new antibiotic from Sorangium cellulosum)

RN 158181-47-6 CAPLUS

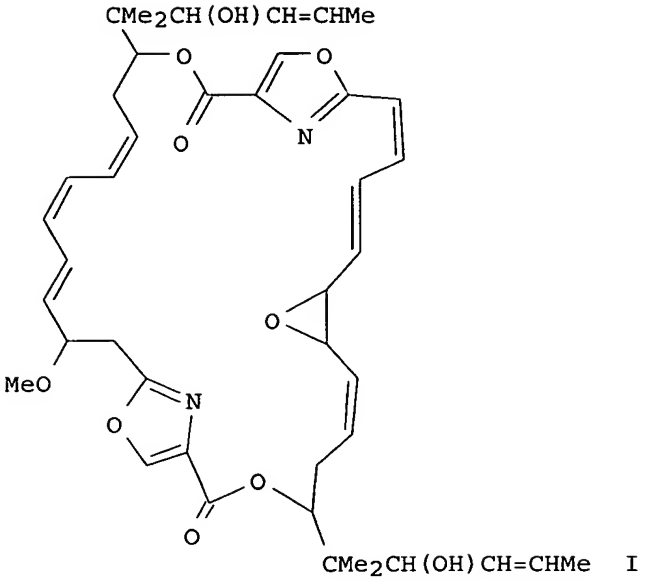
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



L12 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:625972 CAPLUS
DOCUMENT NUMBER: 121:225972
TITLE: Antibiotics from gliding bacteria. LIX. Disorazoles, highly cytotoxic metabolites from the sorangicin-producing bacterium Sorangium cellulosum, strain So ce12
AUTHOR(S): Jansen, Rolf; Irschik, Herbert; Reichenbach, Hans; Wray, Victor; Hoefle, Gerhard
CORPORATE SOURCE: GBF, Gesellschaft fuer Biotechnol. Forschung mbH, Braunschweig, D-38124, Germany
SOURCE: Liebigs Annalen der Chemie (1994), (8), 759-73
CODEN: LACHDL; ISSN: 0170-2041
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

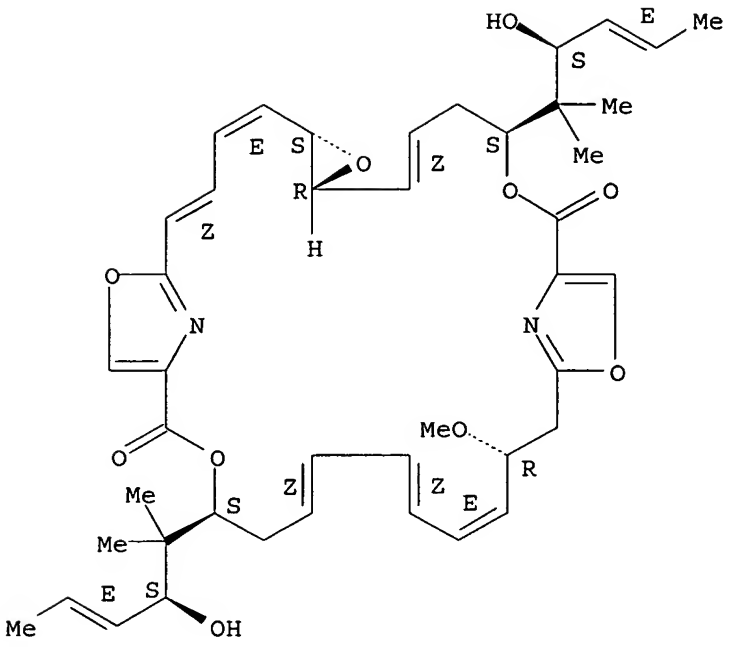
AB Twenty-nine disorazoles A-H were isolated by solvent partitions and chromatog. separation from S. cellulosum, strain So ce12, the producer of the sorangicin antibiotics. The disorazoles proved to be highly cytotoxic and active against fungi. The structures of the main component disorazole A1 (I) and 28 variants were elucidated by 2D-NMR and mass spectroscopy. The disorazoles are macrocyclic dilactones of 2 2-pentadecyloxazol-4-carboxylic acids, which are modified in their C chain by variation of the position and configuration of double bonds and O substituents like epoxide, OH, or Me ether groups. In addition to these, 3 disorazoles are ring-enlarged by lactonization to a more distant OH group. By feeding of 13C-enriched precursors, the biosynthetic origin of the C atoms in I was investigated. C-2 of the oxazole and the attached pentadecyl chain arise from acetate. The geminal Me groups and the MeO group are derived from the Me group of methionine.

IT **158181-47-6**, Disorazole A1
RL: BIOL (Biological study)
(of Sorangium cellulosum, formation and isolation and structure of)

RN 158181-47-6 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

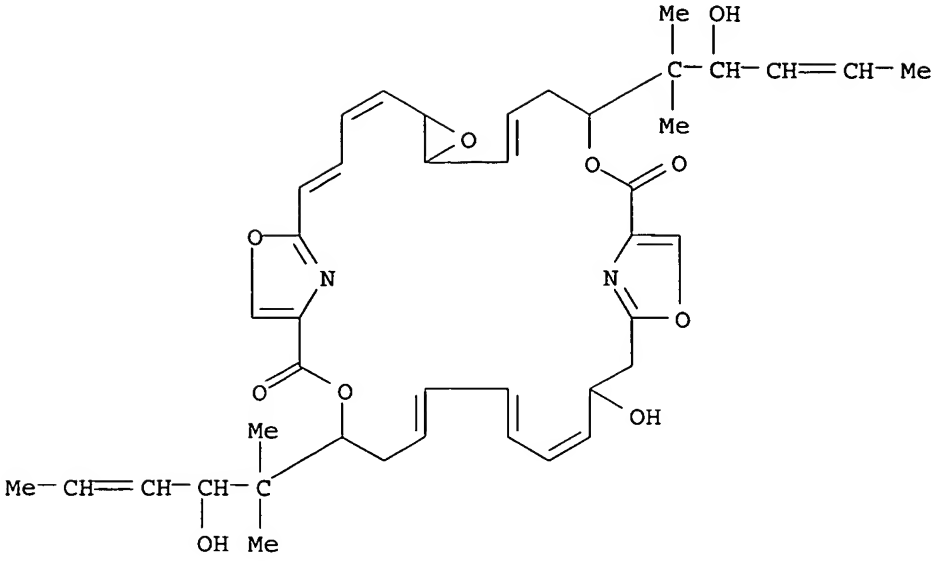
Absolute stereochemistry.
Double bond geometry as described by E or Z.



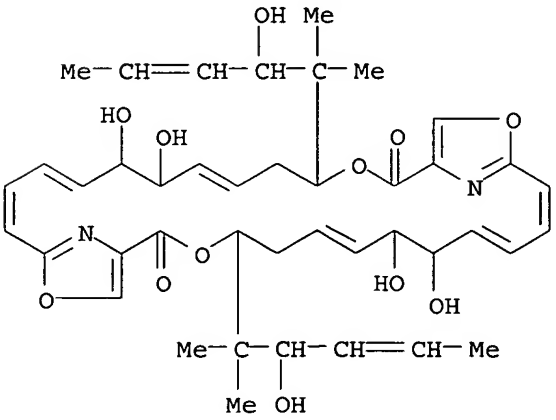
IT **158181-48-7**, Disorazole A2 **158181-49-8**, Disorazole B2
158181-50-1, Disorazole B3 **158181-51-2**, Disorazole B4
158181-52-3, Disorazole C1 **158181-53-4**, Disorazole C2
158181-54-5 **158181-55-6** **158181-56-7**,
Disorazole E1 **158181-57-8**, Disorazole F1 **158181-58-9**,
Disorazole F2 **158181-62-5**, Disorazole H **158181-63-6**,
Disorazole I **158251-66-2**, Disorazole A3 **158251-67-3**,
Disorazole A4 **158251-68-4**, Disorazole A5 **158251-69-5**,
Disorazole A6 **158251-70-8**, Disorazole A7 **158251-71-9**
158251-72-0 **158251-73-1** **158251-74-2**,
Disorazole E2 **158251-75-3**, Disorazole E3 **158251-76-4**,
Disorazole F3 **158252-69-8**, Disorazole B1
RL: BIOL (Biological study)
(of Sorangium cellulosum, isolation and structure of)

RN 158181-48-7 CAPLUS

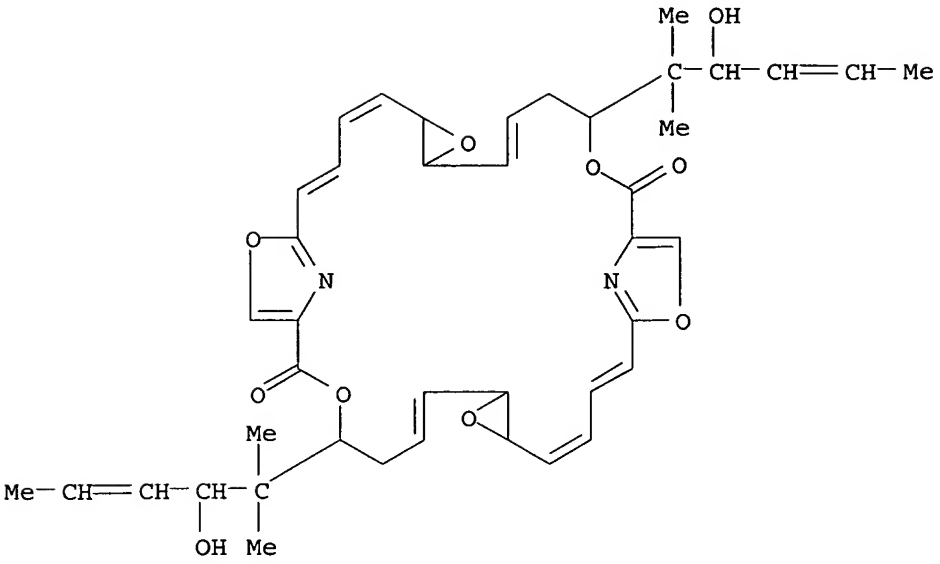
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 20-hydroxy-12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)- (9CI) (CA INDEX NAME)



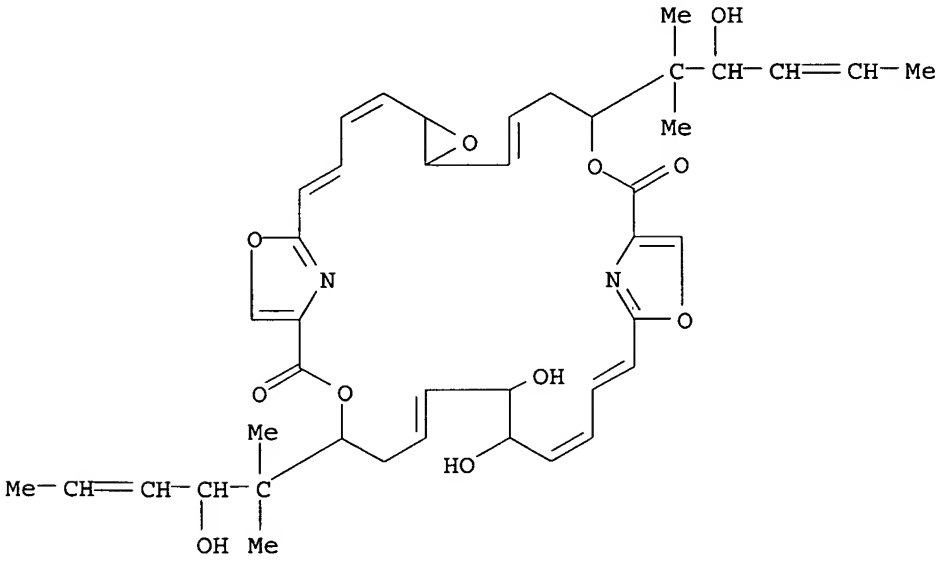
RN 158181-49-8 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,10,12,14(34),16,22,26,28,30(33),32-decaene-2,18-dione, 8,9,24,25-tetrahydroxy-4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)- (9CI) (CA INDEX NAME)



RN 158181-50-1 CAPLUS
CN 7,13,17,24,30,34-Hexaoxa-35,36-diazapentacyclo[30.2.1.115,18.06,8.023,25]hexatriaconta-1(35),2,4,9,15,18(36),19,21,26,32-decaene-14,31-dione, 12,29-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)- (9CI) (CA INDEX NAME)

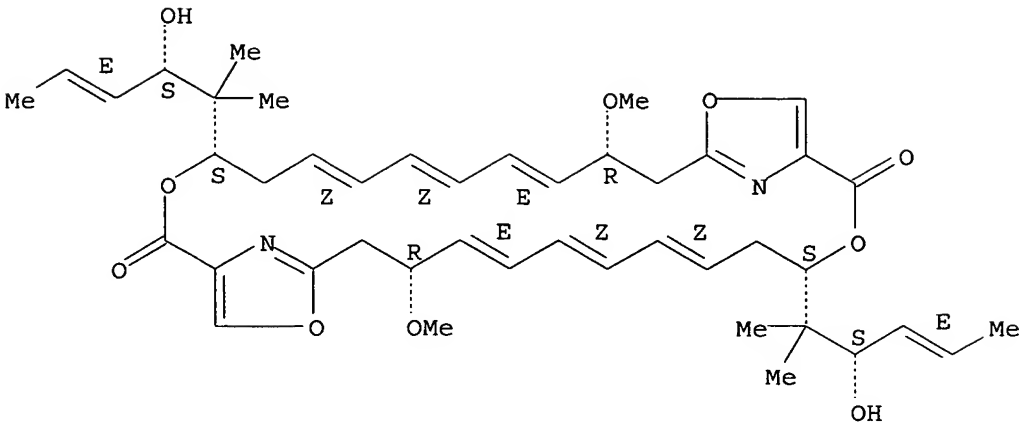


RN 158181-51-2 CAPLUS
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),19,21,25,31-decaene-14,30-dione, 23,24-dihydroxy-12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)- (9CI) (CA INDEX NAME)

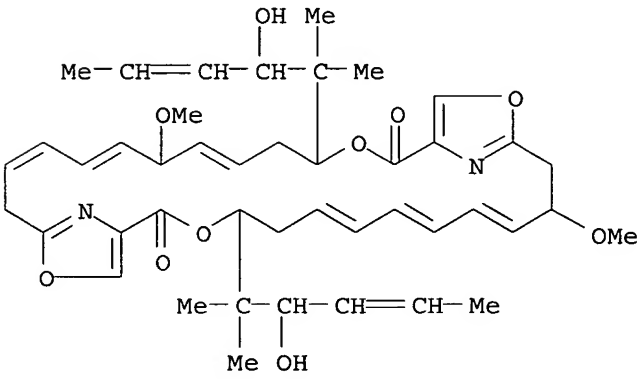


RN 158181-52-3 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,24,26,30(33),32-decaene-2,18-dione, 4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-, (4S,6Z,8Z,10E,12R,20S,22Z,24Z,26E,28R)- (9CI) (CA INDEX NAME)

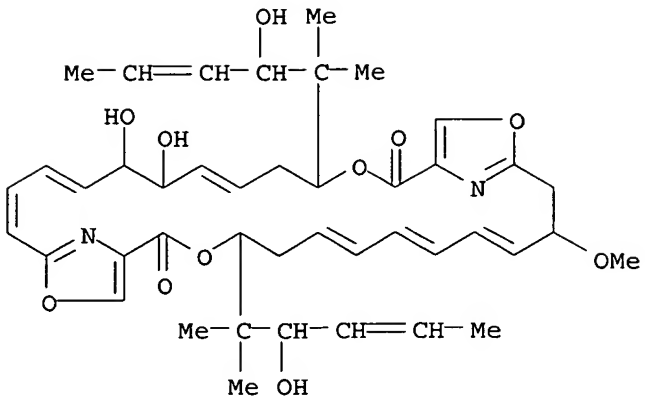
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



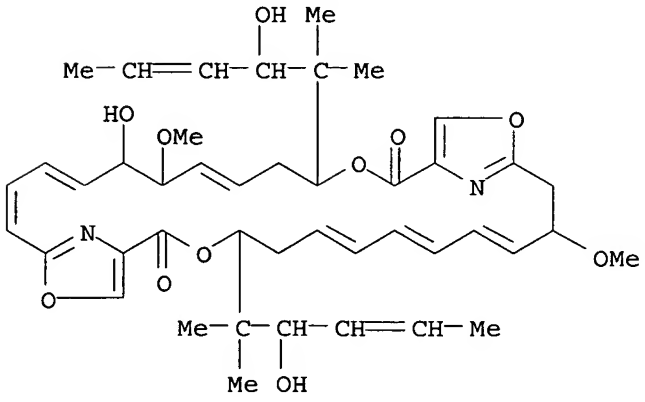
RN 158181-53-4 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,25,27,30(33),32-decaene-2,18-dione, 4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-12,24-dimethoxy- (9CI) (CA INDEX NAME)



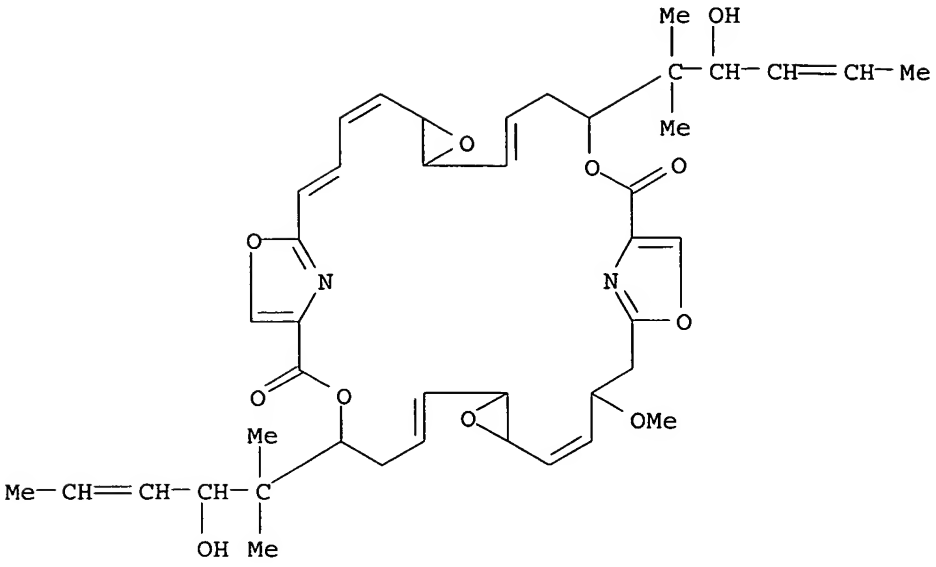
RN 158181-54-5 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,26,28,30(33),32-decaene-2,18-dione, 24,25-dihydroxy-4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-12-methoxy- (9CI) (CA INDEX NAME)



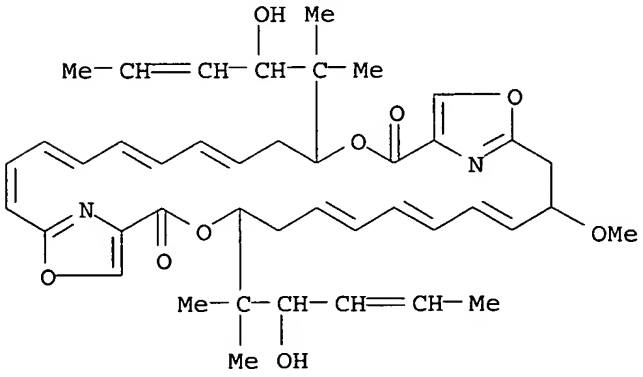
RN 158181-55-6 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,26,28,30(33),32-decaene-2,18-dione, 25-hydroxy-4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-12,24-dimethoxy- (9CI) (CA INDEX NAME)



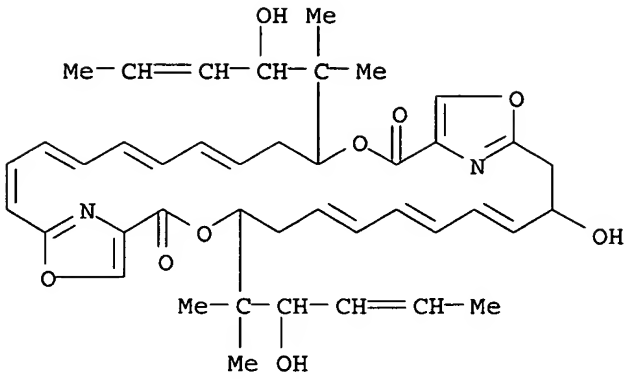
RN 158181-56-7 CAPLUS
CN 7,13,17,24,30,34-Hexaoxa-35,36-diazapentacyclo[30.2.1.115,18.06,8.023,25]hexatriaconta-1(35),2,4,9,15,18(36),21,26,32-nonaene-14,31-dione, 12,29-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)



RN 158181-57-8 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,12,14(34),16,22,24,26,30(33),32-undecaene-2,18-dione, 4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-28-methoxy- (9CI) (CA INDEX NAME)



RN 158181-58-9 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,12,14(34),16,22,24,26,30(33),32-undecaene-2,18-dione, 28-hydroxy-4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)- (9CI) (CA INDEX NAME)



RN 158181-62-5 CAPLUS
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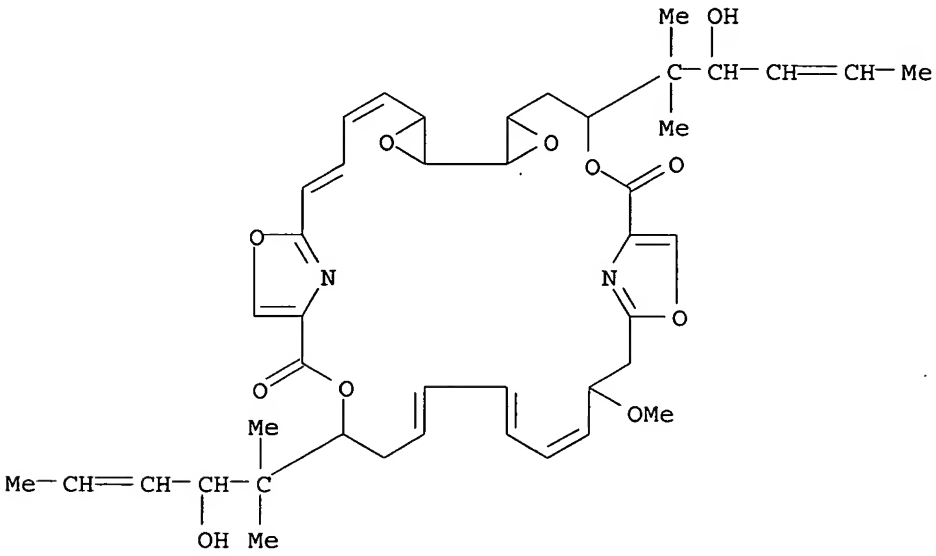

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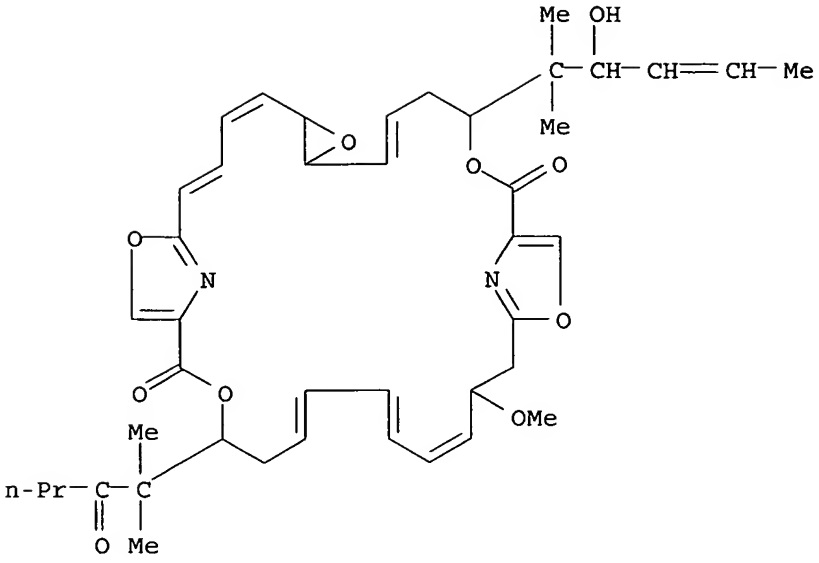

RN 158251-66-2 CAPLUS
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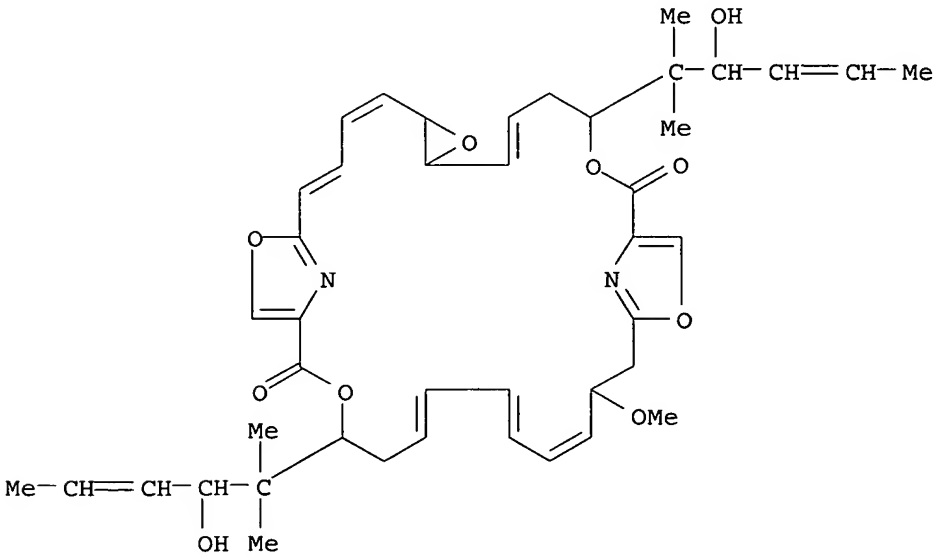
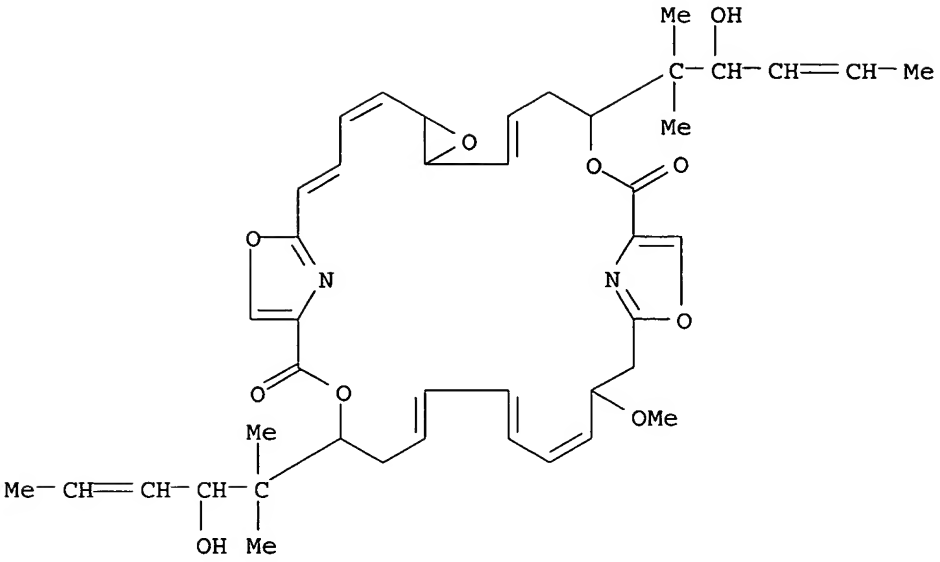
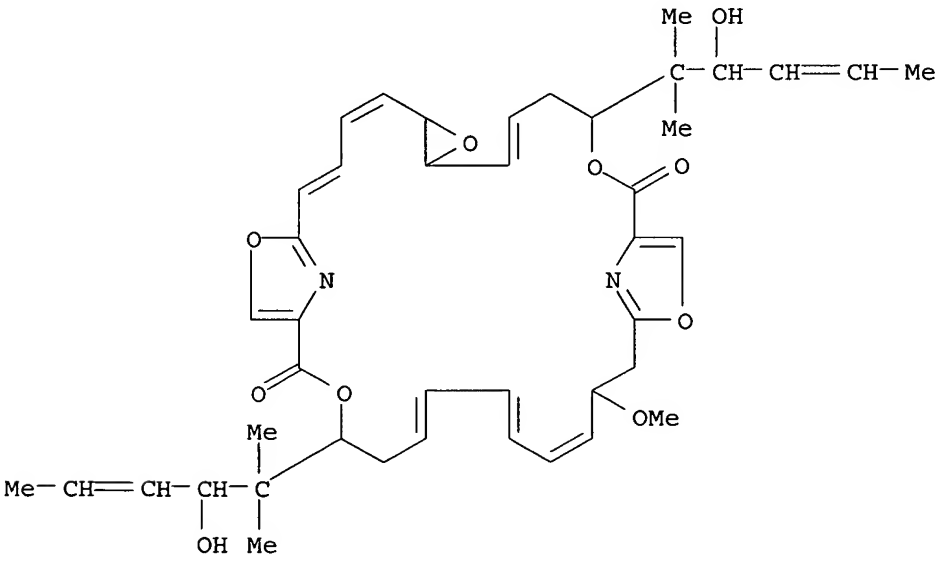


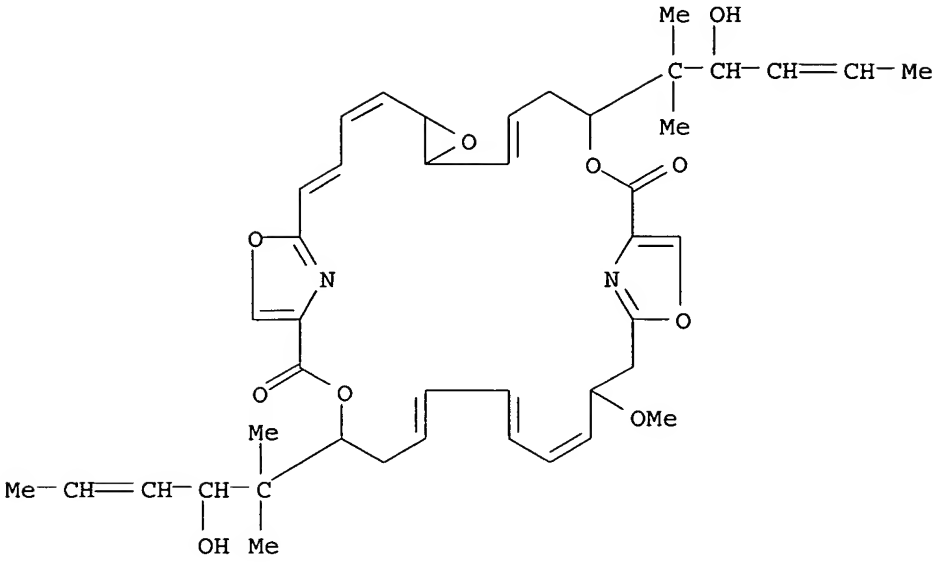
RN 158251-67-3 CAPLUS
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)



RN 158251-68-4 CAPLUS
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)



RN 158251-69-5 CAPLUS
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)



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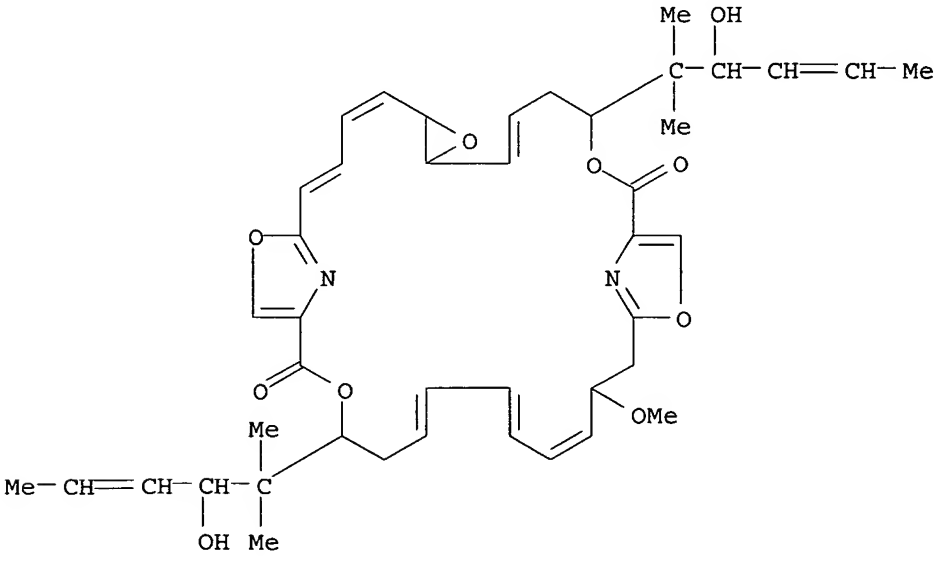
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)



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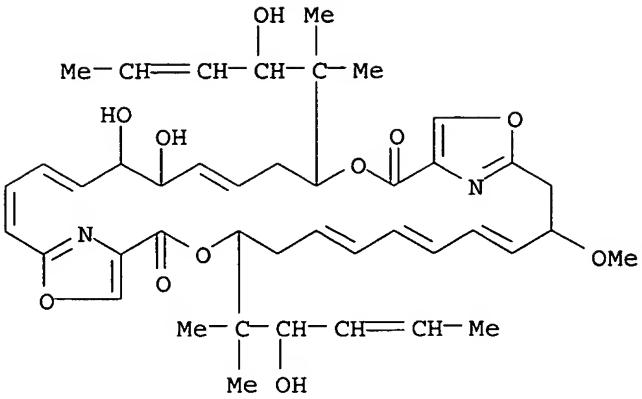
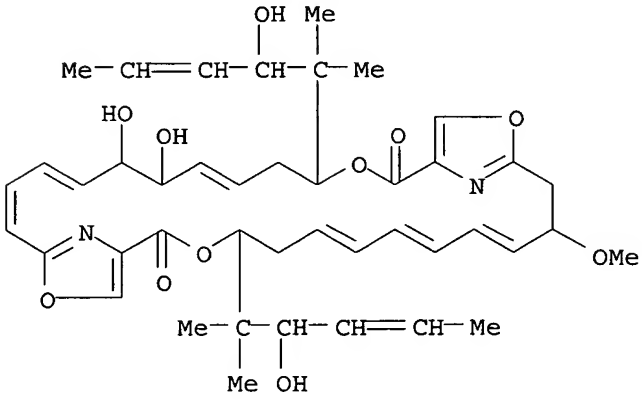
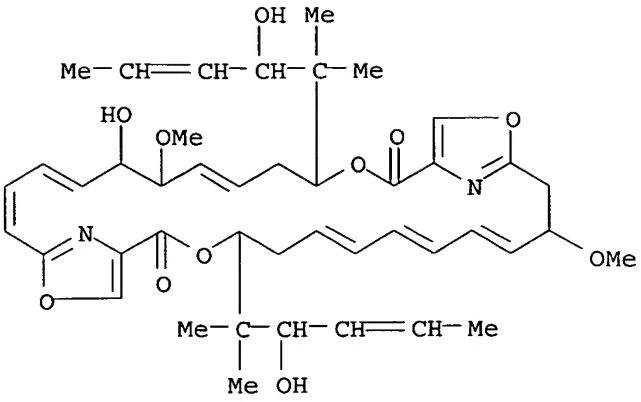


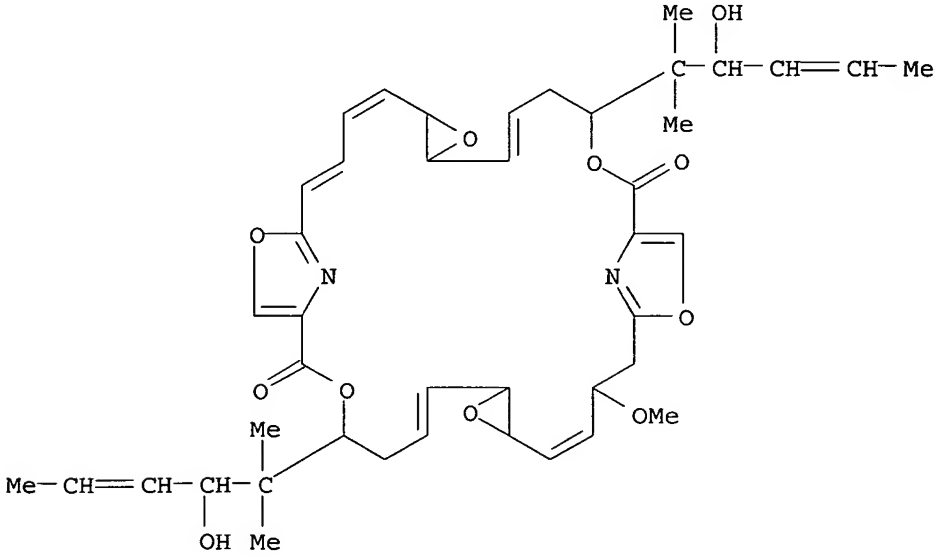
RN 158251-72-0 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,26,28,30(33),32-decaene-2,18-dione, 24,25-dihydroxy-4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-12-methoxy- (9CI) (CA INDEX NAME)



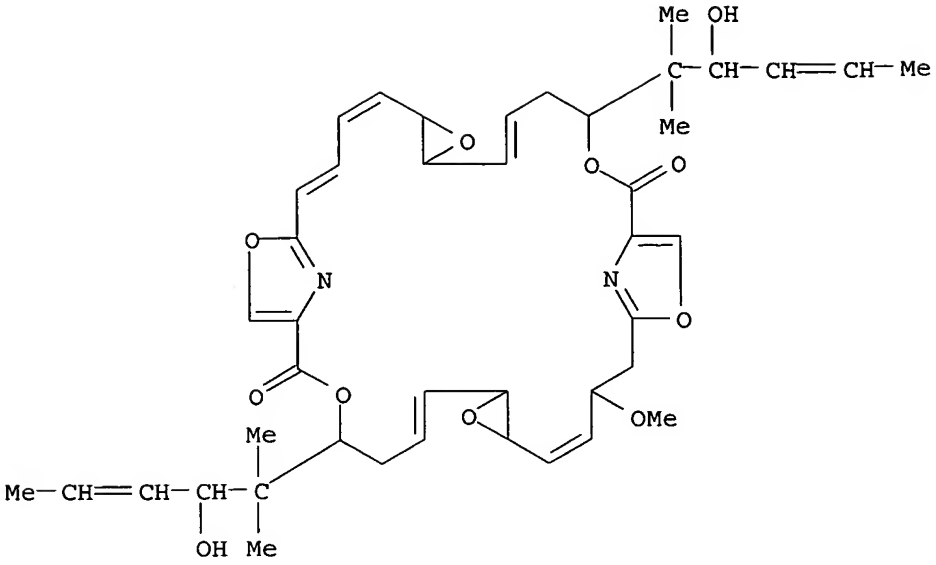
RN 158251-73-1 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,26,28,30(33),32-decaene-2,18-dione, 25-hydroxy-4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-12,24-dimethoxy- (9CI) (CA INDEX NAME)



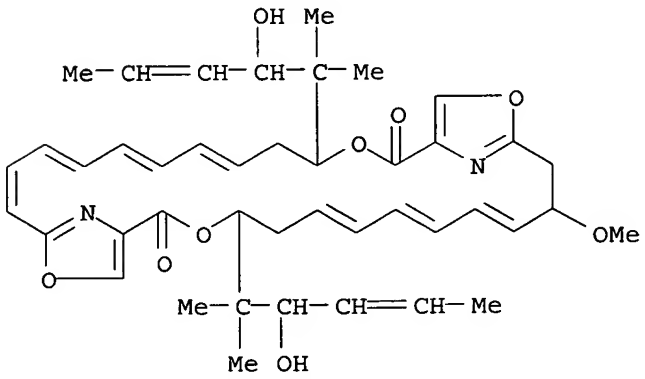
RN 158251-74-2 CAPLUS
CN 7,13,17,24,30,34-Hexaoxa-35,36-diazapentacyclo[30.2.1.115,18.06,8.023,25]hexatriaconta-1(35),2,4,9,15,18(36),21,26,32-nonaene-14,31-dione, 12,29-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)



RN 158251-75-3 CAPLUS
CN 7,13,17,24,30,34-Hexaoxa-35,36-diazapentacyclo[30.2.1.115,18.06,8.023,25]hexatriaconta-1(35),2,4,9,15,18(36),21,26,32-nonaene-14,31-dione, 12,29-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)



RN 158251-76-4 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,12,14(34),16,22,24,26,30(33),32-undecaene-2,18-dione, 4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-28-methoxy- (9CI) (CA INDEX NAME)



RN 158252-69-8 CAPLUS
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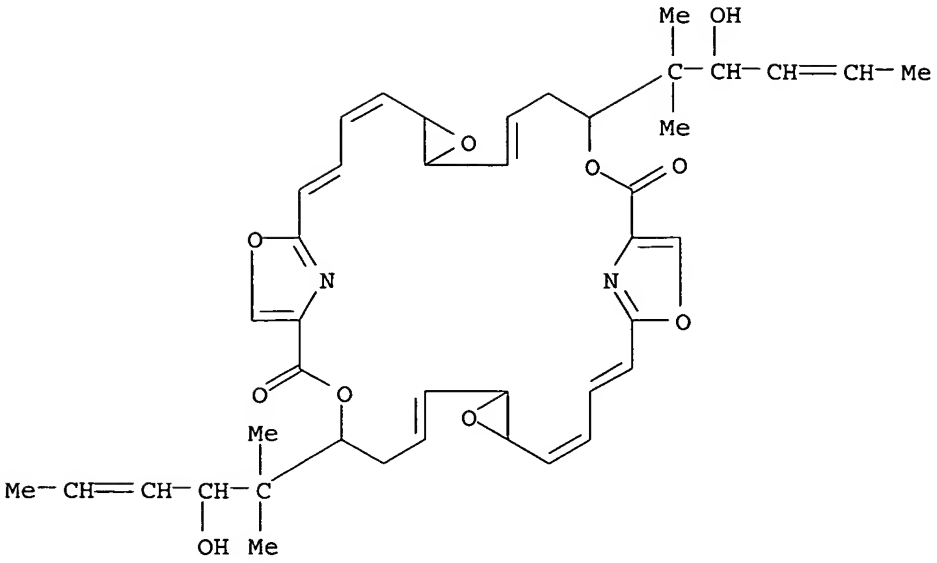

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                 HERBERT"/AU OR "IRSCHIK HERBERT DIPL BIOL"/AU OR "IRSCHIK
                 HERBET"/AU)
L30          225 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("JANSEN R"/AU OR "JANSEN R
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                 OR "JANSEN R K"/AU OR "JANSEN R L H"/AU OR "JANSEN R M W"/AU
                 OR "JANSEN R P"/AU OR "JANSEN R P M"/AU OR "JANSEN R P S"/AU
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                 OR "JANSEN R W M M"/AU OR "JANSEN RALF"/AU OR "JANSEN RALF
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L31           72 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("SASSE F"/AU OR "SASSE F
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L35           13 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L29 AND (L30 OR L31 OR L32 OR
                 L33)) OR (L30 AND (L31 OR L32 OR L33)) OR (L31 AND (L32 OR
                 L33)) OR (L32 AND L33)


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L35  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:252340  CAPLUS
DOCUMENT NUMBER:          140:264487
TITLE:                    Medicaments containing disorazoles and derivatives
                          thereof for the treatment of benign and malignant
                          tumors
INVENTOR(S):              Irschik, Herbert; Jansen, Rolf; Sasse,
                          Florenz; Baasner, Silke; Schmidt,
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Peter; Gunther, Eckhard
PATENT ASSIGNEE(S): Zentaris GmbH, Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024149	A1	20040325	WO 2003-EP9329	20030822
W: AT, AU, BR, BY, CA, CN, CO, GE, HR, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RU, SG, UA, UZ, YU, ZA				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2438001	AA	20040224	CA 2003-2438001	20030822
AU 2003296872	A1	20040430	AU 2003-296872	20030822
US 2004106662	A1	20040603	US 2003-646904	20030822
EP 1536789	A1	20050608	EP 2003-794920	20030822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK				
BR 2003013789	A	20050705	BR 2003-13789	20030822
CN 1678310	A	20051005	CN 2003-820093	20030822
JP 2006500398	T2	20060105	JP 2004-535140	20030822
ZA 2005001196	A	20050901	ZA 2005-1196	20050210
NO 2005001444	A	20050519	NO 2005-1444	20050318
PRIORITY APPLN. INFO.:			US 2002-405594P P	20020824
			WO 2003-EP9329 W	20030822

OTHER SOURCE(S): MARPAT 140:264487
AB The invention discloses disorazole compds. which are used as medicaments, preferably in the treatment of tumors, especially in the case of drug resistance and in metastasizing carcinoma. Possible uses thereof are not restricted to tumor diseases.
IC ICM A61K031-424
ICS C07D498-22; C07D498-18
CC 1-6 (Pharmacology)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:620373 CAPLUS
DOCUMENT NUMBER: 137:124294
TITLE: Pharmaceutically active macrocycles
INVENTOR(S): Gerth, Klaus; Hoefle, Gerhard; **Irschik, Herbert**; Jansen, Rolf; Karama, Usama; Kunze, Brigitte; Leibold, Thomas; Reichenbach, Hans; **Sasse, Florenz**; Schinner, Marc; Soeker, Udo; Steinmetz, Heinrich; Vollbrecht, Larissa; Washausen, Peter; Heusser, Christoph; Oberer, Lukas
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H., Switz.
SOURCE: Brit. UK Pat. Appl., 17 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2367553	A1	20020410	GB 2000-21649	20000904

PRIORITY APPLN. INFO.: GB 2000-21649 20000904
OTHER SOURCE(S): MARPAT 137:124294
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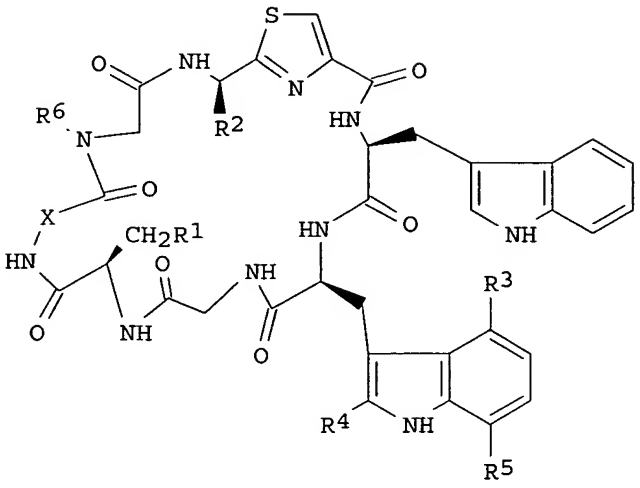

I

AB Compds. (I) are claimed, wherein R1, R2, and R3 independently are H, C1-C4 alkyl which is substituted or unsubstituted by OH, or C1-C4 alkoxy; R4 is H, halogen, C1-C4 alkyl which is substituted or unsubstituted by OH, or C1-C4 alkoxy; R5 is H or halogen; R6 is H or C1-C4 alkyl; and X is C=CH2 or CHR6 wherein R6 is C1-C4 alkyl which is substituted or unsubstituted by -S-C1-C4 alkyl. Compds. I are useful against autoimmune disorders or diseases.

IC ICM C07D513-08
ICS A61K031-429
ICA A61P003-10; A61P011-06; A61P013-00; A61P017-00; A61P029-00; A61P037-00
ICI C07D513-08, C07D259-00, C07D277-00
CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 15

L35 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:52420 CAPLUS
DOCUMENT NUMBER: 118:52420
TITLE: Thiangazole for treatment of viral diseases
INVENTOR(S): Hunsmann, Gerhard; Jurkiewicz, Elke; Reichenbach, Hans; Forche, Edgar; Gerth, Klaus; **Irschik, Herbert**; Kunze, Brigitte; **Sasse, Florenz** ; Hoefle, Gerhard; et al.
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung mbH, Germany; Deutsches Primatenzentrum GmbH
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9211008	A1	19920709	WO 1991-EP2504	19911223
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
DE 4041687	C1	19920813	DE 1990-4041687	19901224
PRIORITY APPLN. INFO.:			DE 1990-4041687 A	19901224

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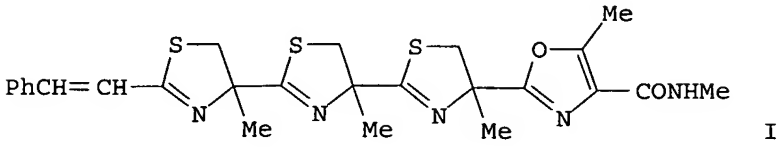


I

AB Thiangazole (I) is useful for the treatment of viral diseases (e.g. HIV virus). Thus, I was isolated by extraction of Polyangium cell mass with acetone and purification by medium-pressure chromatog. The antiviral activity of I at 0.047 nM was demonstrated. The selectivity index was also determined

IC ICM A61K031-425
ICS C07D417-14

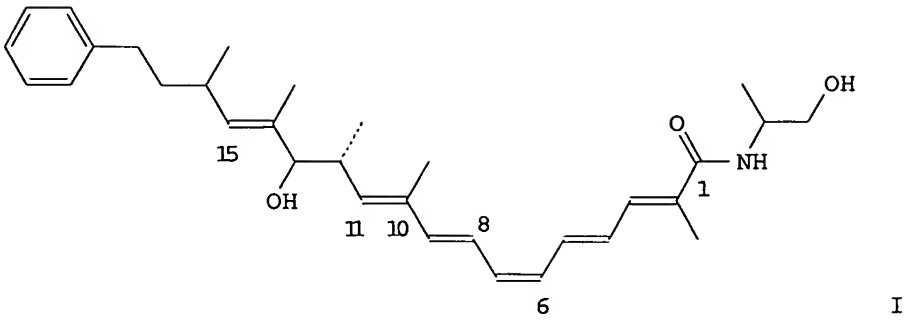
CC 1-5 (Pharmacology)

L35 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:632213 CAPLUS
DOCUMENT NUMBER: 117:232213
TITLE: Manufacture of fenalamides for treatment of viral infections
INVENTOR(S): Hunsmann, Gerhard; Jurkiwicz, Elke; Reichenbach, Hans; Forche, Edgar; Gerth, Klaus; **Irschik, Herbert** ; Kunze, Brigitte; **Sasse, Florenz**; Hoefle, Gerhard; et al.
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H. (GBF), Germany; Deutsches Primatenzentrum G.m.b.H.
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4041688	A1	19920709	DE 1990-4041688	19901224
DE 4041688	C2	19930225		
WO 9211004	A1	19920709	WO 1991-EP2503	19911223
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
PRIORITY APPLN. INFO.:			DE 1990-4041688 A	19901224

GI



I

AB Fenalamides (e.g. I) are manufactured by cultures of Myxococcus stipitatus DSM6259 for use in the treatment of viral infections. Fenalamides are manufactured in cultures in a complete medium containing an adsorbent resin. The fenalamides are eluted from the resin with MeOH and extracted after concentration with EtOAc and final purification by HPLC using a gradient of aqueous MeOH to elute the fractions. Fenalamides were shown to inhibit HIV-1 replication.

IC ICM A61K031-165
ICS C12P013-02

CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 1, 10, 25

L35 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:626295 CAPLUS
DOCUMENT NUMBER: 117:226295
TITLE: Thiangazole, its preparation, compositions, and use thereof
INVENTOR(S): Hoefle, Gerhard; Bedorf, Norbert; Forche, Edgar; Gerth, Klaus; **Irschik, Herbert**; Jansen, Rolf; Kunze, Brigitte; Reichenbach, Hans; **Sasse, Florenz**; et al.
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H., Germany; Ciba-Geigy A.-G.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9211258	A1	19920709	WO 1991-EP2336	19911206
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2097594	AA	19920625	CA 1991-2097594	19911204
AU 9190369	A1	19920722	AU 1991-90369	19911206
AU 659423	B2	19950518		
EP 564479	A1	19931013	EP 1992-900244	19911206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
HU 64337	A2	19931228	HU 1993-1854	19911206

JP 06504197	T2	19940519	JP 1991-500363		19911206
BR 9107189	A	19940927	BR 1991-7189		19911206
US 5604249	A	19970218	US 1995-487382		19950607
US 5610038	A	19970311	US 1995-487385		19950607
US 5622979	A	19970422	US 1995-487384		19950607
PRIORITY APPLN. INFO.:			DE 1990-4041685	A	19901224
			WO 1991-EP2336	A	19911206
			US 1993-78159	B3	19930917
			US 1994-286309	B3	19940805

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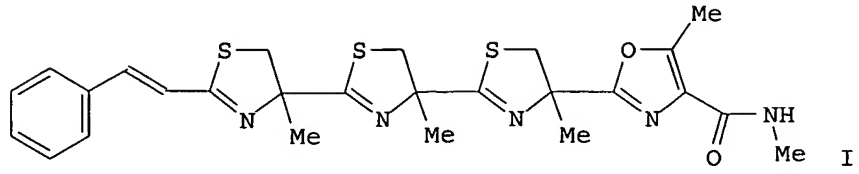
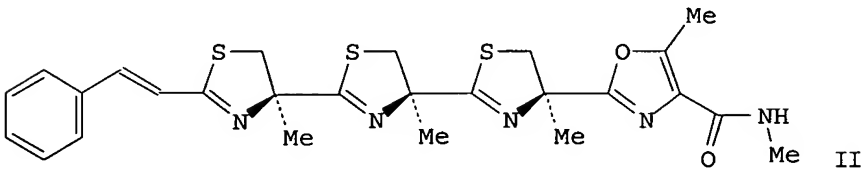


I



II

AB Compds. I and especially II (referred to as thiangazole), and their pharmaceutically acceptable salts, are provided, as are processes for their preparation, therapeutic, pesticide, and crop-protection compns. containing them. Thiangazole was isolated from cultures of Polyangium Pl 3007 and characterized. The anthelmintic activity of thiangazole is described (e.g. in nematode-infested sheep and in pea seedlings infested with Aphis craccivora), as are a variety of formulations (dusts, granules, tablets, injections, etc.).

IC ICM C07D417-14
ICS C07D413-14; C12P017-16; A61K031-425; A61K031-42; A01N043-78; A01N043-76; A01N063-02

ICI C07D417-14, C07D277-00, C07D263-00

CC 1-5 (Pharmacology)
Section cross-reference(s): 5, 10, 16, 63

L35 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1992:571426 CAPLUS
DOCUMENT NUMBER:	117:171426
TITLE:	phenoxan, a method for its preparation and its use as antibiotic, fungicide and parasiticide
INVENTOR(S):	Reichenbach, Hans; Forche, Edgar; Gerth, Klaus; **Irschik, Herbert**; Kunze, Brigitte; **Sasse, Florenz**; Hoefle, Gerhard; Bedorf, Norbert; Jansen, Rolf; et al.
PATENT ASSIGNEE(S):	Gesellschaft fuer Biotechnologische Forschung m.b.H. (GBF), Germany
SOURCE:	Ger. Offen., 5 pp. CODEN: GWXXBX

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4041282	A1	19920702	DE 1990-4041282	19901221
WO 9211257	A1	19920709	WO 1991-EP2440	19911218
W: AU, CA, FI, HU, JP, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9190688	A1	19920722	AU 1991-90688	19911218
ZA 9110053	A	19920826	ZA 1991-10053	19911220
PRIORITY APPLN. INFO.:			DE 1990-4041282 A	19901221
			WO 1991-EP2440 A	19911218

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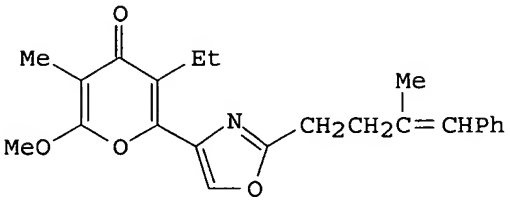

I

AB Phenoxan (I) as prepared in a medium containing Polyangium DSM 6270 is claimed. Pharmaceuticals containing I for the treatment of diseases caused by fungi or parasites (no data) are claimed. A bioreactor was charged with a nutrient medium and Polyangium PI VO19 and aerated to give I. I had activity as antibiotic and fungicide.

IC ICM C07D413-04
ICS A01N043-76; A61K031-42; C12P017-16
ICI C07D413-04, C07D309-30, C07D263-32; C12P017-16, C12R001-01
CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 10, 16

L35 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:563856 CAPLUS
DOCUMENT NUMBER: 117:163856
TITLE: Fermentatively manufactured phenoxan for the treatment of viral diseases
INVENTOR(S): Hunsmann, Gerhard; Jurkiwicz, Elke; Reichenbach, Hans; Forche, Edgar; Gerth, Klaus; **Irschik, Herbert** ; Kunze, Brigitte; **Sasse, Florenz**; Hoefle, Gerhard; et al.
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H., Germany; Deutsches Primatenzentrum G.m.b.H.
SOURCE: Ger. Offen., 7 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4041281	A1	19920702	DE 1990-4041281	19901221
DE 4041281	C2	19950309		
WO 9211006	A1	19920709	WO 1991-EP2481	19911220
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				

PRIORITY APPLN. INFO.: DE 1990-4041281 A 19901221

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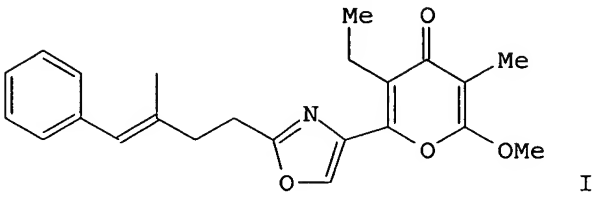

I

AB Phenoxan (I), prepared by fermentation of Polyangium, is a virucide. I is suitable for treatment of retroviral diseases, such as AIDS. At 6.6 μM, I totally inhibited the infection of MT-4 cells (Harada et al., 1986) by human immunodeficiency virus 1.

IC ICM A61K031-42

CC 1-5 (Pharmacology)
Section cross-reference(s): 16

L35 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:530034 CAPLUS

DOCUMENT NUMBER: 115:130034

TITLE: Fermentative manufacture of fungicidal nitrogen-containing ambruticines

INVENTOR(S): Bedorf, Norbert; Forche, Edgar; Gerth, Klaus; Hoefle, Gerhard; **Irschik, Herbert**; Jansen, Rolf; Kunze, Brigitte; Reichenbach, Hans; **Sasse, Florenz**; et al.

PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H. (GBF), Germany

SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9100860	A1	19910124	WO 1990-EP1082	19900705
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
DE 3922283	C1	19910516	DE 1989-3922283	19890706
EP 438554	A1	19910731	EP 1990-910646	19900705
EP 438554	B1	19940608		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 03503773	T2	19910822	JP 1990-510287	19900705
AT 106880	E	19940615	AT 1990-910646	19900705
ES 2055914	T3	19940901	ES 1990-910646	19900705

PRIORITY APPLN. INFO.: DE 1989-3922283 A 19890706
EP 1990-910646 A 19900705
WO 1990-EP1082 W 19900705

OTHER SOURCE(S): MARPAT 115:130034

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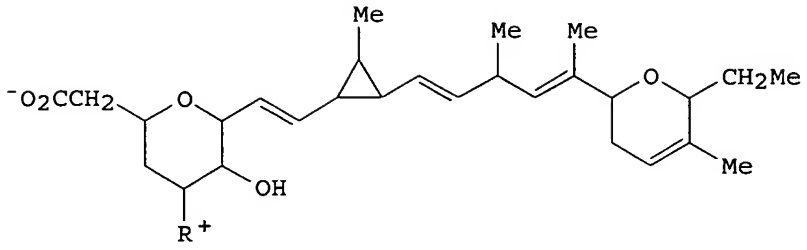

I

AB The N-containing ambruticins I (R = NMe3, NHMe2, NH2Me, NH3) and their salts are prepared as agrochem. and medical fungicides, by the fermentation of Sorangium cellulosum. Aerobic fermentation of S. cellulosum, in the presence of Amberlite XAD-1180 gave a mixture of I, which was eluted from the resin with MeOH. I inhibited the growth of Botrytis cinerea, Candida albicans, other fungi and yeasts, in vitro.

IC ICM C07D309-22
ICS A61K031-35; A01N043-16

CC 5-2 (Agrochemical Bioregulators)
Section cross-reference(s): 16, 63

L35 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:205552 CAPLUS
DOCUMENT NUMBER: 114:205552
TITLE: Manufacture of antibiotic nannochelins with Nannocystics exedens and its purification
INVENTOR(S): Reichenbach, Hans; Bedorf, Norbert; Forche, Edgar; Gerth, Klaus; Hoefle, Gerhard; **Irschik, Herbert**; Jansen, Rolf; Kunze, Brigitte; **Sasse, Florenz**; et al.
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H. (GBF), Germany
SOURCE: Ger., 4 pp.
CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3932095	C1	19901025	DE 1989-3932095	19890926

PRIORITY APPLN. INFO.: DE 1989-3932095 19890926
OTHER SOURCE(S): MARPAT 114:205552
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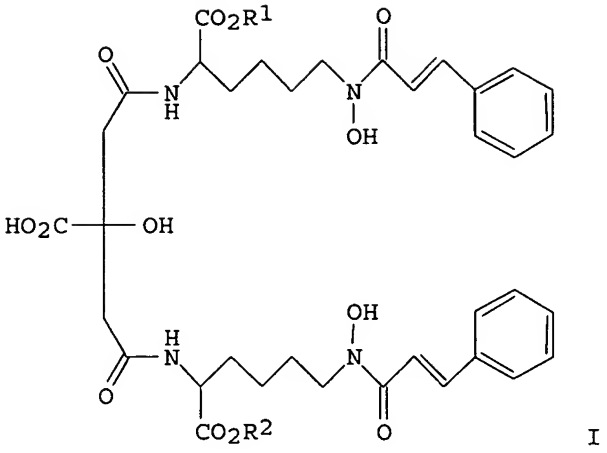

I

AB Nannochelins ([I]; R1, R2 = independently Me, H) are manufactured by fermentation of Nannocystis exedens and purified chromatog. These compds. are active as antibiotics against Gram-pos. bacteria. N. exedens were cultured in a peptone/salts culture medium for 3-4 days at 30°. I was recovered by stirring the ion-exchange resin XAD into the medium and eluting bound material with a MeOH/H2O mixture followed by elution with MeOH. This second eluate contained I, and after extraction with benzene and concentration this fraction was fractionated by chromatog. on Sephadex LH-20, followed by chromatog. on Vieselogol RP018 and XAD resin to recover nannochelins A, B, and C. In vivo testing showed the compds. to be effective against Brevibacterium ammoniagenes (min. inhibitory concentration 1.5 μg/mL) and Staphylococcus aureus at 25 μg/mL. The compds. also showed some activity against yeast and Escherichia coli.

IC ICM C07C259-06
ICS C12N001-20; A61K031-71; C07C233-51; C12P013-02

CC 16-4 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 10

L35 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1990:457461 CAPLUS
DOCUMENT NUMBER:	113:57461
TITLE:	Fungicidal steroids from Trichoderma
INVENTOR(S):	Reichenbach, Hans; Forche, Edgar; Gerth, Klaus; **Irschik, Herbert**; Kunze, Brigitte; **Sasse, Florenz**; Hoefle, Gerhard; Augustiniak, Hermann; Bedorf, Norbert; et al.
PATENT ASSIGNEE(S):	Gesellschaft fuer Biotechnologische Forschung m.b.H. (GBF), Germany
SOURCE:	Ger. Offen., 9 pp. CODEN: GWXXBX
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 3823068	A1	19900111	DE 1988-3823068	19880707
PRIORITY APPLN. INFO.:			DE 1988-3823068	19880707
OTHER SOURCE(S):	MARPAT 113:57461			

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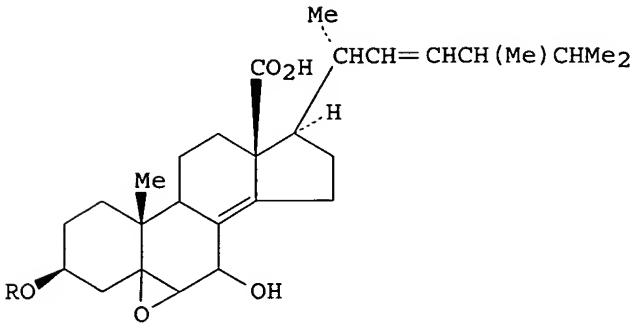


I, R=COCH(NHSO3Na)CH(OH)CHMe2

II, R=H

AB Ergokonins A (I) and B (II) are produced by fermentation with Trichoderma koningii. Thus, a preculture was inoculated into 70 L medium containing 25 g melt extract, 5 g cellulose, and 3 g peptone/L and incubated at 30° with stirring and aeration for 5 days. The initial pH was brought to 5.5 with HOAc and maintained with HOAc during fermentation The products were isolated by solvent extraction and purified by chromatog. on silica gel and DEAE-cellulose and by HPLC. Yields of I and II were 46 and 280 mg, resp. I and II inhibited yeast and mycelial fungi, with I having .apprx.10-fold the activity of II.

IC ICM C07J009-00
ICS C12N001-20; B01D011-04; B01D015-08

ICI C12P001-02, C12R001-885

CC 16-2 (Fermentation and Bioindustrial Chemistry)

L35 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1990:438902 CAPLUS
DOCUMENT NUMBER:	113:38902
TITLE:	Antibiotic So ce38-A
INVENTOR(S):	Reichenbach, Hans; Forche, Edgar; Gerth, Klaus; **Irschik, Herbert**; Kunze, Brigitte; **Sasse, Florenz**; Hoefle, Gerhard; Bedorf, Norbert; Jansen, Rolf; et al.
PATENT ASSIGNEE(S):	Gesellschaft fuer Biotechnologische Forschung m.b.H. (GBF), Germany
SOURCE:	Ger. Offen., 4 pp. CODEN: GWXXBX
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

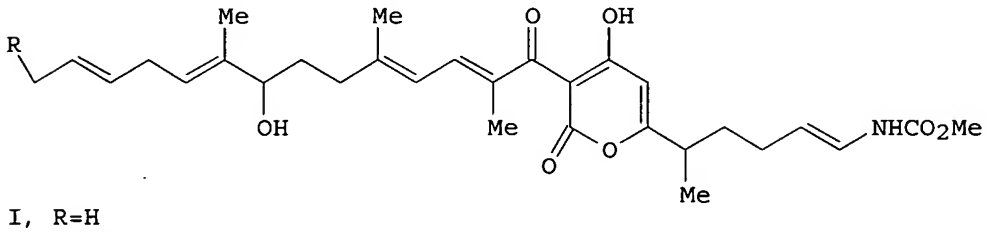
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 3823067 A1 19900111 DE 1988-3823067 19880707
PRIORITY APPLN. INFO.: DE 1988-3823067 19880707

AB Antibiotic So ce38-A (I) is produced by fermentation with Sorangium cellulosum. Thus, a preculture was inoculated into 60 L pH 7.4 medium containing 0.5% glucose, 0.5% Probion, 0.05% MgSO4, and 0.05% CaCl2 and incubated at 32° with stirring and aeration. After 4 days, 0.5% glucose was added and fermentation was continued for 2 days. I was extracted from the cell and medium with organic solvents and purified by ion-exchange chromatog. and mol. exclusion chromatog. The yield of I was 1.5 g. It inhibited yeasts and filamentous fungi.

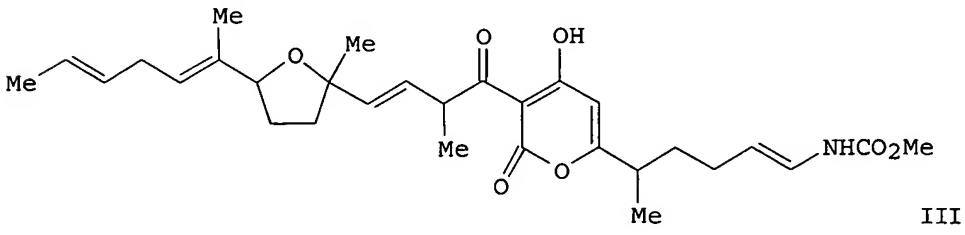
IC ICM C12P001-04
ICS C07G011-00; A61K035-74
ICA C12N001-20
CC 16-2 (Fermentation and Bioindustrial Chemistry)

L35 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:163434 CAPLUS
DOCUMENT NUMBER: 102:163434
TITLE: Antibiotics from gliding bacteria. 25. The corallopyronins, new inhibitors of bacterial RNA synthesis from Myxobacteria
AUTHOR(S): **Irschik, H.; Jansen, R.**; Hoefle, G.; Gerth, K.; Reichenbach, H.
CORPORATE SOURCE: Dep. Microbiol., GBF, Ges. Biotechnol. Forsch., Braunschweig, D-3300, Fed. Rep. Ger.
SOURCE: Journal of Antibiotics (1985), 38(2), 145-52
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=H

II, R=Me



III

AB From the culture broth of the myxobacterium, Corallococcus (Myxococcus) coralloides, 3 new antibiotics were isolated: corallopyronins A (I), B

(II), and C (III). The compds., which are chemical related to the recently discovered myxopyronins, act mainly on gram-pos. bacteria, with min. inhibitory concns. (MIC) values of 0.1-10 μg/mL, and only exceptionally or at much higher concns. (MIC ≥100 μg/mL) on gram-negatives. They do not inhibit eukaryotic organisms and show no toxicity for mice when administered s.c. The corallopyronins appear to block specifically eubacterial RNA polymerase.
CC 10-1 (Microbial Biochemistry)

L35 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:572497 CAPLUS
DOCUMENT NUMBER: 99:172497
TITLE: The myxalamids, new antibiotics from Myxococcus xanthus (Myxobacterales). I. Production, physico-chemical and biological properties, and mechanism of action
AUTHOR(S): Gerth, K.; **Jansen, R.**; Reifenstahl, G.; Hoefle, G.; **Irschik, H.**; Kunze, B.; Reichenbach, H.; Thierbach, G.
CORPORATE SOURCE: Abt. Mikrobiol., Ges. Biotechnol. Forsch., Braunschweig, D-3300, Fed. Rep. Ger.
SOURCE: Journal of Antibiotics (1983), 36(9), 1150-6 CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
AB From the cell mass and culture supernatant fraction of M. xanthus strain Mx X12, an antibiotic activity against yeasts, molds, and some gram-pos. bacteria could be extracted It consisted of 4 biol. active compds. which were named myxalamid A, B, C, and D. The main component, myxalamid B, blocked the submitochondrial particle respiratory chain of beef heart at the site of complex I, i.e. NADH:ubiquinone oxidoreductase. The myxalamids are new antibiotics.
CC 10-1 (Microbial Biochemistry)

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L30 225 SEA FILE=CAPLUS ABB=ON PLU=ON ("JANSEN R"/AU OR "JANSEN R A"/AU OR "JANSEN R C"/AU OR "JANSEN R E"/AU OR "JANSEN R F"/AU OR "JANSEN R H"/AU OR "JANSEN R H J"/AU OR "JANSEN R H S"/AU OR "JANSEN R J"/AU OR "JANSEN R J E"/AU OR "JANSEN R J J"/AU OR "JANSEN R K"/AU OR "JANSEN R L H"/AU OR "JANSEN R M W"/AU OR "JANSEN R P"/AU OR "JANSEN R P M"/AU OR "JANSEN R P S"/AU OR "JANSEN R T P"/AU OR "JANSEN R W"/AU OR "JANSEN R W M"/AU OR "JANSEN R W M M"/AU OR "JANSEN RALF"/AU OR "JANSEN RALF P"/AU OR "JANSEN RALF PETER"/AU OR "JANSEN RALPH"/AU)
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L41 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:53914 CAPLUS
DOCUMENT NUMBER: 144:150233
TITLE: Preparation of 1,2,3,4-tetrahydrocarbazoles as gonadotropin-releasing hormone receptor (LHRH) antagonist
INVENTOR(S): Paulini, Klaus; Gerlach, Matthias; Guenther, Eckhard; Polymeropoulos, Emmanuel; **Baasner, Silke**; Schmidt, Peter; Kuehne, Ronald; Soederhaell, Arvid
PATENT ASSIGNEE(S): Zentaris G.m.b.H., Germany; Solvay Pharmaceuticals B.V.
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006005484	A1	20060119	WO 2005-EP7255	20050705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
DE 102004033902	A1	20060216	DE 2004-102004033902	20040714
US 2006014818	A1	20060119	US 2005-172142	20050630
PRIORITY APPLN. INFO.:			DE 2004-102004033902A	20040714
			US 2004-587969P P	20040714
			US 2005-683178P P	20050520

OTHER SOURCE(S): MARPAT 144:150233
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X1 = S, O; X2, X3 = O with provisos; R1, R2 = H, aryl, alkyl, etc.; R3 = alkyl, arylalkyl, heteroarylalkyl, etc.; R4, R5, R6, R7 = H, halo, CN, etc.; R9 = H, alkyl, aryl, etc.; R10 = R11, COR11, CO2R11, etc.; R11 = alkyl, aryl, heteroaryl, etc.; R8 = alkylaryl, alkylheteroaryl, etc.;] and their pharmaceutically acceptable salts were prepared For example, tetrahydrocarbazole II was prepared via solid phase synthesis from FmocValOH in 14% yield. In LHRH receptor binding assays, 7-examples of compds. I exhibited EC50 values ranging from 80-1.0 x 10-10 M.
IC ICM C07D209-82

ICS A61K031-403; A61P015-00; A61P035-00; A61P043-00
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
IT Prostate gland, disease
(**benign** hyperplasia, treatment of; preparation of tetrahydrocarbazoles as gonadotropin-releasing hormone receptor (LHRH) antagonist)
IT Hyperplasia
(**benign** prostatic, treatment of; preparation of tetrahydrocarbazoles as gonadotropin-releasing hormone receptor (LHRH) antagonist)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:252340 CAPLUS
DOCUMENT NUMBER: 140:264487
TITLE: Medicaments containing disorazoles and derivatives thereof for the treatment of **benign** and malignant tumors
INVENTOR(S): **Irschik, Herbert**; Jansen, Rolf; **Sasse, Florenz**; **Baasner, Silke**; Schmidt, Peter; Gunther, Eckhard
PATENT ASSIGNEE(S): Zentaris GmbH, Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004024149	A1	20040325	WO 2003-EP9329		20030822
W: AT, AU, BR, BY, CA, CN, CO, GE, HR, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RU, SG, UA, UZ, YU, ZA					
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
CA 2438001	AA	20040224	CA 2003-2438001		20030822
AU 2003296872	A1	20040430	AU 2003-296872		20030822
US 2004106662	A1	20040603	US 2003-646904		20030822
EP 1536789	A1	20050608	EP 2003-794920		20030822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK					
BR 2003013789	A	20050705	BR 2003-13789		20030822
CN 1678310	A	20051005	CN 2003-820093		20030822
JP 2006500398	T2	20060105	JP 2004-535140		20030822
ZA 2005001196	A	20050901	ZA 2005-1196		20050210
NO 2005001444	A	20050519	NO 2005-1444		20050318
PRIORITY APPLN. INFO.:			US 2002-405594P	P	20020824
			WO 2003-EP9329	W	20030822

OTHER SOURCE(S): MARPAT 140:264487
AB The invention discloses disorazole compds. which are used as medicaments, preferably in the treatment of tumors, especially in the case of drug resistance and in metastasizing carcinoma. Possible uses thereof are not restricted to tumor diseases.
IC ICM A61K031-424

ICS C07D498-22; C07D498-18
CC 1-6 (Pharmacology)
IT Inflammation
(Crohn's disease; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Intestine, disease
(Crohn's; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Ovary, neoplasm
(adenocarcinoma; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Allergy
Inflammation
Nose, disease
(allergic rhinitis; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Drug resistance
(antitumor; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases, and use with other agents)
IT Lung, neoplasm
(carcinoma; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Uterus, neoplasm
(cervix, carcinoma; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Carcinoma
(cervix; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Carcinoma
(colon adenocarcinoma; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Intestine, neoplasm
(colon, adenocarcinoma; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Intestine, neoplasm
(colon; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT AIDS (disease)
Allergy
Allergy inhibitors
Analgesics
Anti-AIDS agents
Anti-infective agents
Anti-inflammatory agents
Antiarteriosclerotics
Antiarthritics
Antiasthmatics
Antimalarials
Antipyretics
Antitumor agents
Arteriosclerosis
Arthritis
Asthma
Brain, neoplasm

Cachexia
Drug delivery systems
Eczema
Eosinophil
Gastrointestinal agents
Human
Infection
Inflammation
Keratosis
Kidney, neoplasm
Liver, neoplasm
Lung, neoplasm
Malaria
Mammary gland, neoplasm
Multiple sclerosis
Neoplasm
Nervous system agents
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Psoriasis
Respiratory system, disease
Skin, neoplasm
(disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)

IT Cell cycle
Cytotoxic agents
Immunomodulators
Multidrug resistance
(disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases, and use with other agents)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases, and use with other agents)

IT Drug delivery systems
(emulsions; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)

IT Drug delivery systems
(foams; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)

IT Neuroglia, neoplasm
(glioblastoma; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)

IT Drug delivery systems
(implants; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)

IT Fever and Hyperthermia
Pain
(infection-related; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)

IT Signal transduction, biological
(inhibitors; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases, and use with other agents)

IT Drug delivery systems
(ointments; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)

IT Carcinoma

(ovarian adenocarcinoma; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Drug delivery systems
(pastes; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Medical goods
(plasters; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Disease, animal
(proliferative; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Carcinoma
(pulmonary; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Antitumor agents
(resistance to; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases, and use with other agents)
IT Drug delivery systems
(solns.; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Drug delivery systems
(suspensions; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT Tubulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-, polymerization; disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases, and use with other agents)
IT 158181-56-7, Disorazole E1 674799-35-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases)
IT 50-18-0, Cyclophosphamide 51-21-8, 5-FU 57-22-7, Vincristine 59-05-2, Methotrexate 3778-73-2, Ifosfamide 15663-27-1, Cisplatin 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 41575-94-4, Carboplatin 53643-48-4, Vindesine 114977-28-5, Docetaxel 158181-47-6, Disorazole A1 158181-54-5, Disorazole D1 180288-69-1, Herceptin 184475-35-2, Iressa 220127-57-1, Glivec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disorazoles and derivs. for treatment of **benign** and malignant tumors and other diseases, and use with other agents)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

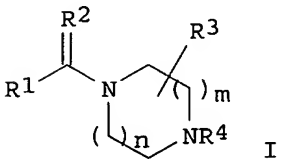
L41 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:20666 CAPLUS
DOCUMENT NUMBER: 140:77166
TITLE: Preparation of arylcarbonylpiperazines and heteroarylcarbonylpiperazines for treating **benign** and malignant tumor diseases
INVENTOR(S): Emig, Peter; Gerlach, Matthias; Polymeropoulos, Emmanuel; Mueller, Gilbert; Schmidt, Peter; **Baasner, Silke**; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris Gmbh, Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002965	A1	20040108	WO 2003-EP6555	20030620
W: AU, BR, BY, CA, CN, CO, GE, HR, HU, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, UA, UZ, YU, ZA				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
AU 2003246571	A1	20040119	AU 2003-246571	20030620
EP 1517898	A1	20050330	EP 2003-761482	20030620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012294	A	20050412	BR 2003-12294	20030620
CN 1665792	A	20050907	CN 2003-815485	20030620
NZ 537916	A	20051125	NZ 2003-537916	20030620
JP 2005538968	T2	20051222	JP 2004-516632	20030620
CA 2433983	AA	20031229	CA 2003-2433983	20030627
US 2004097734	A1	20040520	US 2003-608520	20030627
ZA 2004009610	A	20050418	ZA 2004-9610	20041126
NO 2005000428	A	20050125	NO 2005-428	20050125

PRIORITY APPLN. INFO.: US 2002-393027P P 20020629
WO 2003-EP6555 W 20030620

OTHER SOURCE(S): MARPAT 140:77166
GI



I

AB Title compds. [I; R1 = (substituted) fluoren-9-one, isoxazolyl, cinnolinyl, isothiazolyl, isoquinolinyl, 9H-fluorenyl, 9H-xanthenyl, 1H-pyrazolyl; R2 = O, S; R3 = H, (substituted) alkyl, halo, CO2H, CONH2; R4 = (substituted) (hetero)aryl, alkylaryl, alkylhetaryl; m, n = 0-3], were prepared Thus, 9-fluorenone-4-carbonyl chloride in DMF was successively treated with N-methylmorpholine, 1-(3,5-dimethoxyphenyl)piperazine, and 1-benzotriazolyltripyrrolidinophosphonium hexafluorophosphate followed by stirring for 12 h at room temperature to give 79,3% 4-[4-(3,5-dimethoxyphenyl)piperazine-1-carbonyl]fluoren-9-one. The latter inhibited proliferation in XTT cytotoxicity test in human tumor cells with EC50 = 0,2-0,555 μg/mL.

IC ICM C07D241-04
ICS C07D405-06; C07D403-06; C07D417-06; C07D413-06; A61K031-497; A61P035-04

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT Tubulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(polymerization, inhibition of; preparation of arylcarbonylpiperazines and heteroarylcarbonylpiperazines for treating **benign** and malignant tumor diseases)

IT Antitumor agents
Human
(preparation of arylcarbonylpiperazines and heteroarylcarbonylpiperazines for treating **benign** and malignant tumor diseases)

IT Neoplasm
(treatment; preparation of arylcarbonylpiperazines and heteroarylcarbonylpiperazines for treating **benign** and malignant tumor diseases)

IT 640286-86-8P 640286-87-9P 640286-88-0P 640286-89-1P 640286-90-4P
640286-91-5P 640286-92-6P 640286-93-7P 640286-94-8P 640286-95-9P
640286-96-0P 640286-97-1P 640286-98-2P 640286-99-3P 640287-00-9P
640287-01-0P 640287-02-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylcarbonylpiperazines and heteroarylcarbonylpiperazines for treating **benign** and malignant tumor diseases)

IT 82-07-5, Xanthene-9-carboxylic acid 1133-77-3 7071-83-2, 9-Fluorenone-4-carbonyl chloride 16015-71-7, 1-(3-Methoxyphenyl)piperazine 53557-93-0, 1-(3,5-Dimethoxyphenyl)piperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of arylcarbonylpiperazines and heteroarylcarbonylpiperazines for treating **benign** and malignant tumor diseases)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:325255
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

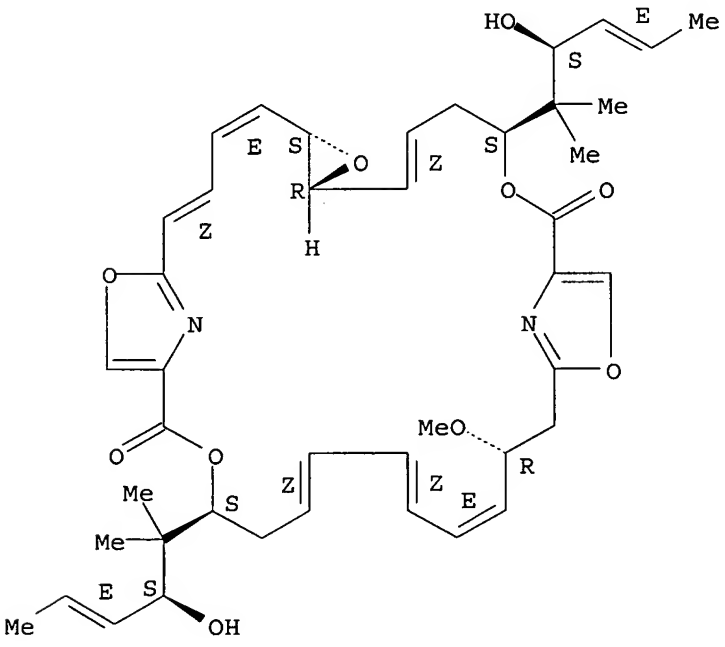
AB A highly convergent asym. synthesis of the masked southern segment of the antimitotic agent disorazole A1, I, involves a Sonogashira coupling between a C1'-C10' enyne II and a suitably protected C11'-C19' vinyl iodide III. The central E,Z,Z-triene moiety is masked as a more stable ynediene.

IT **158181-47-6P**, Disorazole A1 **158181-52-3P**, Disorazole C1
RL: PNU (Preparation, unclassified); PREP (Preparation)
(asym. synthesis of masked southern segment of disorazole A1 and C1 via Sonogashira coupling of vinyl iodide with oxazolyl enyne derivative)

RN 158181-47-6 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 158181-52-3 CAPLUS

CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,24,26,30(33),32-decaene-2,18-dione, 4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-,

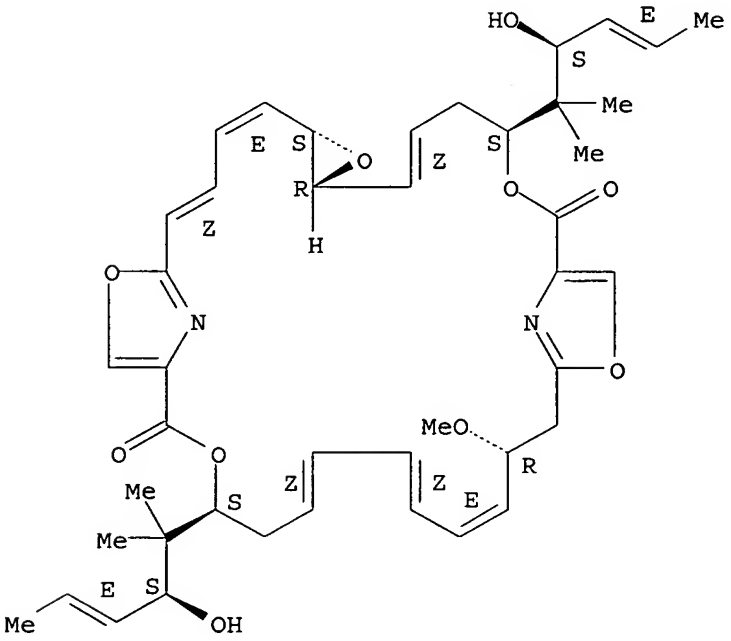
AB The stereoselective synthesis of the masked northern half (I) of the antimitotic natural product disorazole A1 is described involving as key step a Z-selective Wittig olefination of a C1-C11 epoxy aldehyde with a C12-C19 phosphonium iodide.

IT **158181-47-6P**, Disorazole A1
RL: PNU (Preparation, unclassified); PREP (Preparation)
(asym. synthesis of the masked northern half of disorazole A1 via Z-selective Wittig olefination)

RN 158181-47-6 CAPLUS

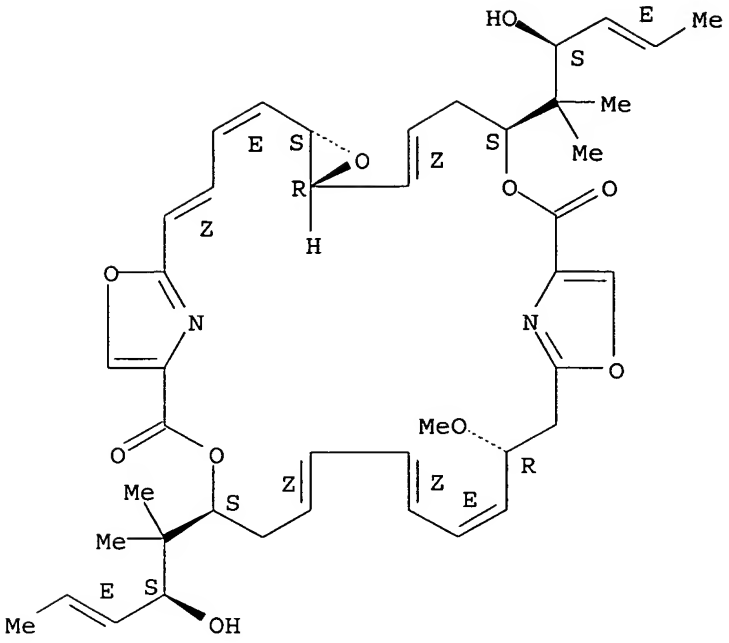
CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



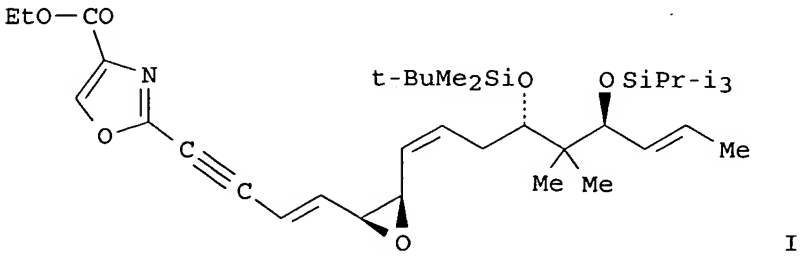
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:640974 CAPLUS
DOCUMENT NUMBER: 137:325255
TITLE: Toward the Total Synthesis of Disorazole A1 and C1: Asymmetric Synthesis of a Masked Southern Segment
AUTHOR(S): Hartung, Ingo V.; Niess, Barbara; Haustedt, Lars Ole; Hoffmann, H. Martin R.
CORPORATE SOURCE: Department of Organic Chemistry, University of Hannover, Hannover, D-30167, Germany
SOURCE: Organic Letters (2002), 4(19), 3239-3242
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:732771 CAPLUS
DOCUMENT NUMBER: 140:41931
TITLE: Toward the total synthesis of disorazole A1: Asymmetric synthesis of the masked northern half
AUTHOR(S): Hartung, Ingo V.; Eggert, Ulrike; Haustedt, Lars Ole; Niess, Barbara; Schaefer, Peter M.; Hoffmann, H. Martin R.
CORPORATE SOURCE: Department of Organic Chemistry, University of Hannover, Hannover, 30167, Germany
SOURCE: Synthesis (2003), (12), 1844-1850
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:41931
GI



I

CORPORATE SOURCE: GBF, Department of Natural Product Biology, German Research Centre for Biotechnology, Braunschweig, D-38124, Germany
SOURCE: Biochemical Pharmacology (2004), 67(5), 927-935
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

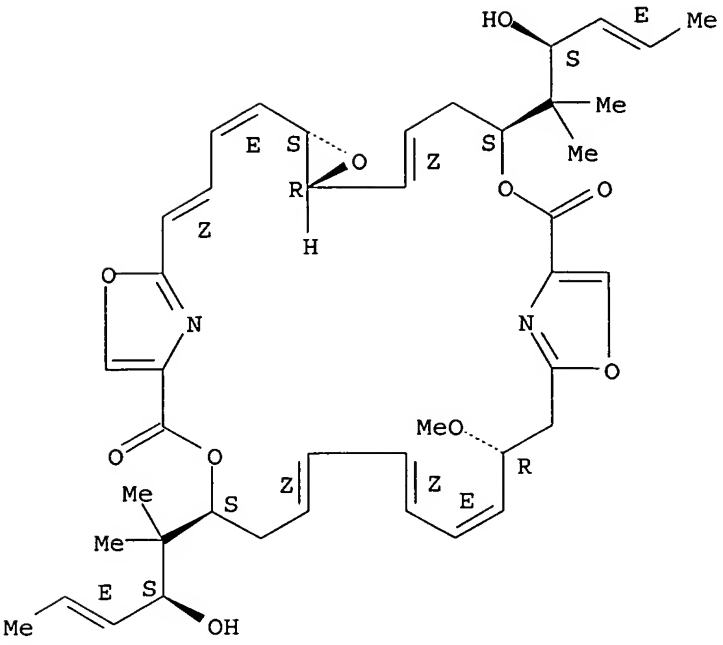
AB Disorazol A1, a macrocyclic polyketide compound that is produced by the mycobacterium Sorangium cellulosum showed a remarkably high cytostatic activity. It inhibited the proliferation of different cancer cell lines including a multidrug-resistant KB line at low picomolar levels. In presence of disorazol A1, the nuclei of the cells increased in size and the cells often became multinucleate. Low concns. of disorazol (<100 pM) induced an apoptotic process, characterized by enhanced caspase-3 activity and DNA laddering, and abnormal, multipolar mitotic spindles. Low concns. also induced an accumulation of p53 protein in the nucleus. At higher concns., we observed an accumulation of the cells in the G2/M-phase of the cell cycle, and a depletion of microtubules. In vitro, disorazol A1 inhibited the polymerization of tubulin in a concentration-dependent manner and independently of microtubule-associated proteins. Correspondingly it induced a complete depolymn. of microtubules prepared in vitro. Formation of defined degradation structures was not observed Disorazol is a novel, highly effective antimitotic agent. Efforts are going on to develop it as an anticancer drug.

IT **158181-47-6**, Disorazol A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disorazol A1 acting on tubulin polymerization and inducing apoptosis in mammalian cells)

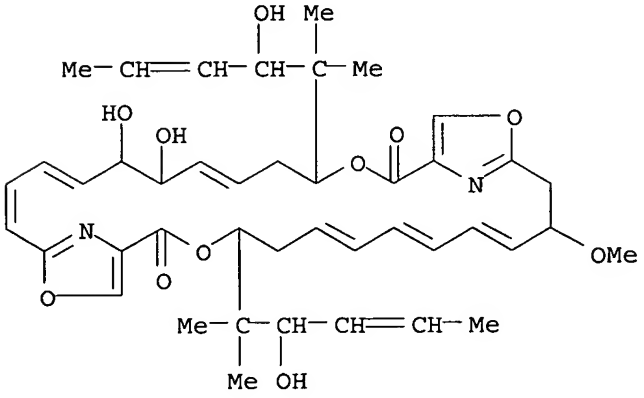
RN 158181-47-6 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

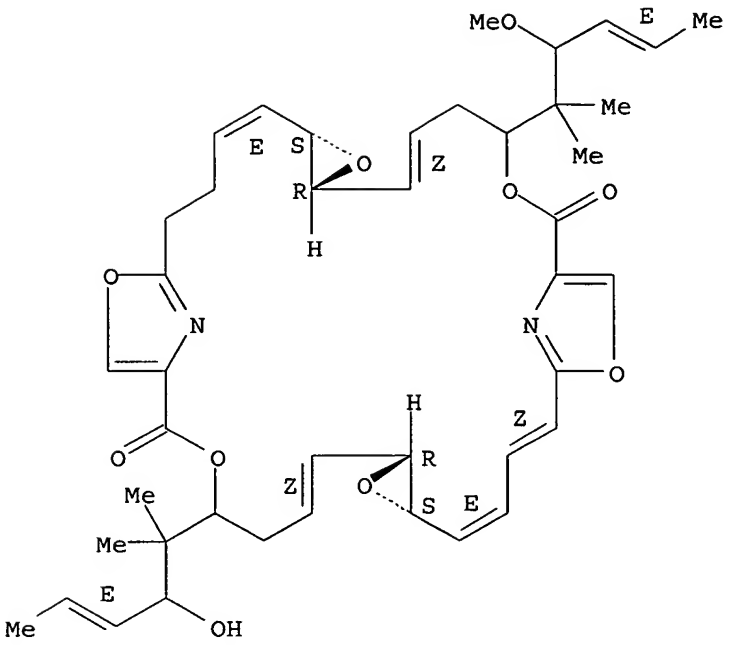


RN 158181-54-5 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,8,10,14(34),16,22,26,28,30(33),32-decaene-2,18-dione, 24,25-dihydroxy-4,20-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-12-methoxy-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:111554 CAPLUS
DOCUMENT NUMBER: 140:385603
TITLE: Disorazol A1, a highly effective antimitotic agent acting on tubulin polymerization and inducing apoptosis in mammalian cells
AUTHOR(S): Elnakady, Yasser A.; Sasse, Florenz; Lunsdorf, Heinrich; Reichenbach, Hans



IT **158181-47-6**, Disorazole A1 **158181-54-5**, Disorazole D1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disorazoles and derivs. for treatment of benign and malignant tumors and other diseases, and use with other agents)

RN 158181-47-6 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

WO 2003-EP9329 W 20030822

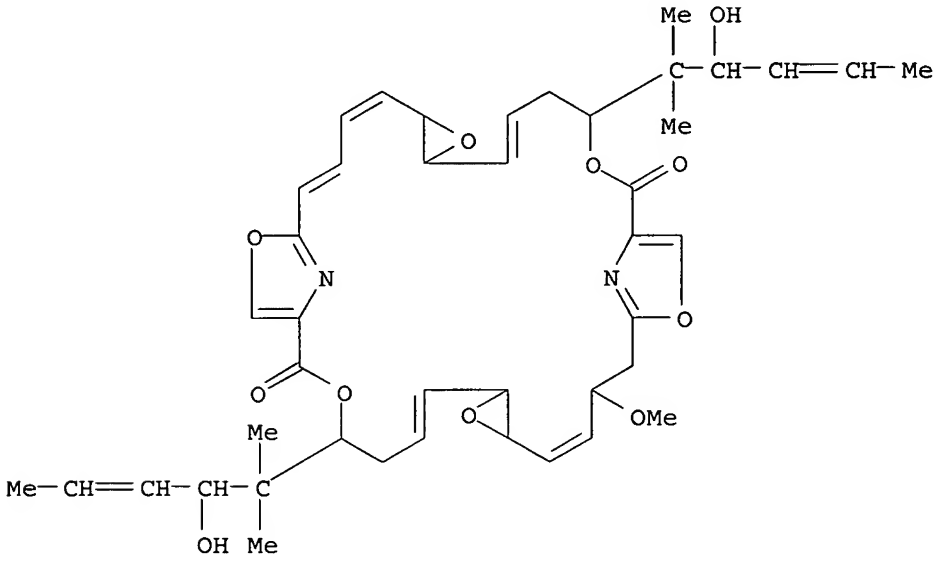
OTHER SOURCE(S): MARPAT 140:264487

AB The invention discloses disorazole compds. which are used as medicaments, preferably in the treatment of tumors, especially in the case of drug resistance and in metastasizing carcinoma. Possible uses thereof are not restricted to tumor diseases.

IT **158181-56-7**, Disorazole E1 **674799-35-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disorazoles and derivs. for treatment of benign and malignant tumors and other diseases)

RN 158181-56-7 CAPLUS

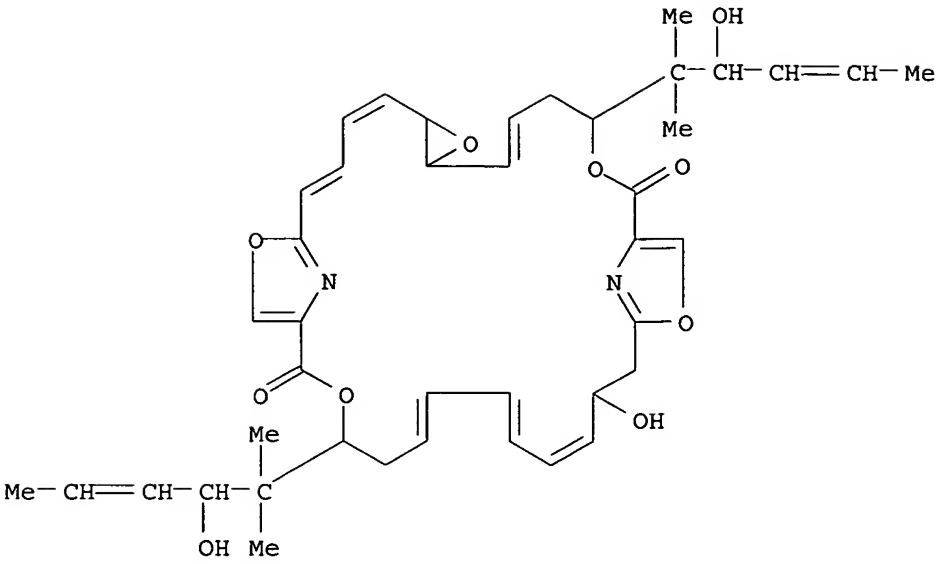
CN 7,13,17,24,30,34-Hexaoxa-35,36-diazapentacyclo[30.2.1.115,18.06,8.023,25]hexatriaconta-1(35),2,4,9,15,18(36),21,26,32-nonaene-14,31-dione, 12,29-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)



RN 674799-35-0 CAPLUS

CN 7,13,17,24,30,34-Hexaoxa-35,36-diazapentacyclo[30.2.1.115,18.06,8.023,25]hexatriaconta-1(35),2,4,9,15,18(36),21,26,32-nonaene-14,31-dione, 12-[(3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-29-[(3E)-2-methoxy-1,1-dimethyl-3-pentenyl]-, (2Z,4E,6R,8S,9Z,21E,23R,25S,26Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as described by E or Z.
Currently available stereo shown.



L12 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:252340 CAPLUS
DOCUMENT NUMBER: 140:264487
TITLE: Medicaments containing disorazoles and derivatives thereof for the treatment of benign and malignant tumors
INVENTOR(S): Irschik, Herbert; Jansen, Rolf; Sasse, Florenz; Baasner, Silke; Schmidt, Peter; Gunther, Eckhard
PATENT ASSIGNEE(S): Zentaris GmbH, Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024149	A1	20040325	WO 2003-EP9329	20030822
W: AT, AU, BR, BY, CA, CN, CO, GE, HR, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RU, SG, UA, UZ, YU, ZA				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2438001	AA	20040224	CA 2003-2438001	20030822
AU 2003296872	A1	20040430	AU 2003-296872	20030822
US 2004106662	A1	20040603	US 2003-646904	20030822
EP 1536789	A1	20050608	EP 2003-794920	20030822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK				
BR 2003013789	A	20050705	BR 2003-13789	20030822
CN 1678310	A	20051005	CN 2003-820093	20030822
JP 2006500398	T2	20060105	JP 2004-535140	20030822
ZA 2005001196	A	20050901	ZA 2005-1196	20050210
NO 2005001444	A	20050519	NO 2005-1444	20050318

PRIORITY APPLN. INFO.: US 2002-405594P P 20020824

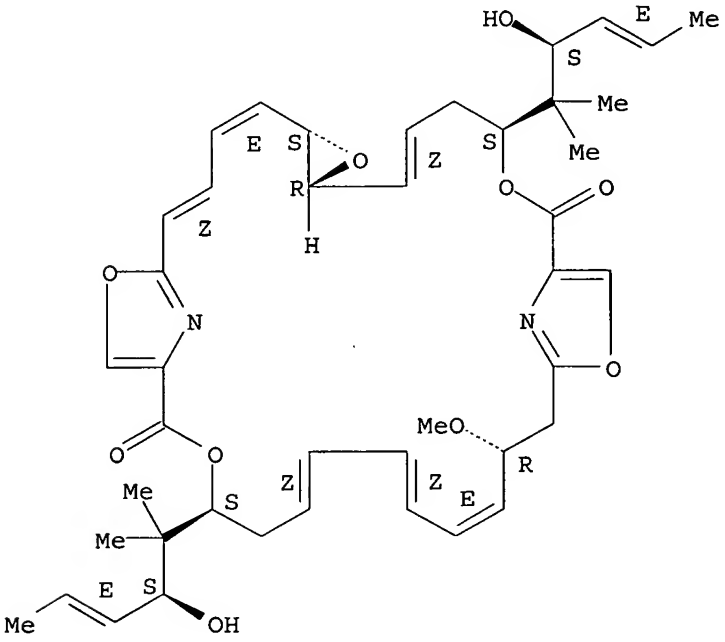
CL02 and CP70 as against the corresponding sensitive cells.

IT **158181-47-6**, Disorazole A1 **158181-48-7**, Disorazole A2
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); BIOL (Biological study); OCCU (Occurrence)
(isolation of antibiotics effective on multidrug-resistant cancer cells from Sorangium cellulosum)

RN 158181-47-6 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)-20-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

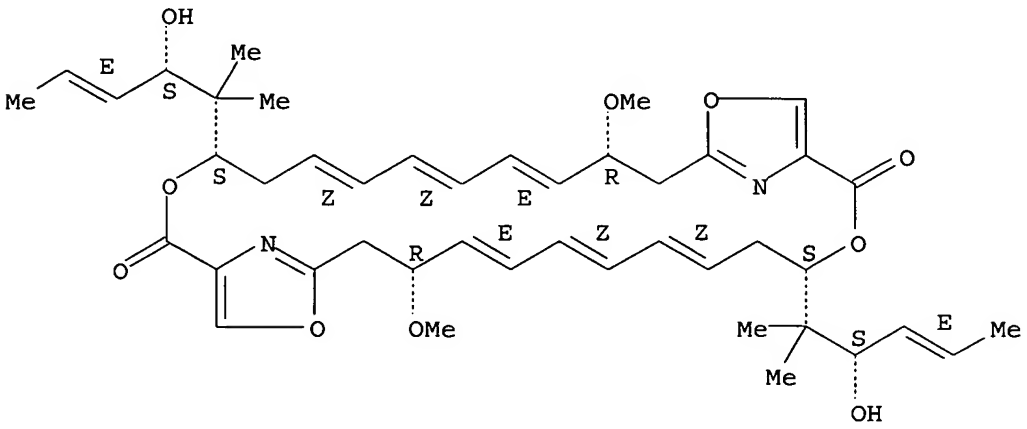


RN 158181-48-7 CAPLUS

CN 7,13,17,29,33-Pentaoxa-34,35-diazatetracyclo[29.2.1.115,18.06,8]pentatriaconta-1(34),2,4,9,15,18(35),21,23,25,31-decaene-14,30-dione, 20-hydroxy-12,28-bis(2-hydroxy-1,1-dimethyl-3-pentenyl)- (9CI) (CA INDEX NAME)

6,8,10,14(34),16,22,24,26,30(33),32-decaene-2,18-dione,
4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-,
(4S,6Z,8Z,10E,12R,20S,22Z,24Z,26E,28R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.

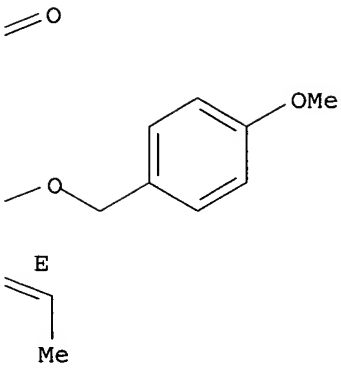


REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:387479 CAPLUS
DOCUMENT NUMBER: 142:16295
TITLE: Isolation of antibiotics effective on multidrug-resistant cancer cells from Sorangium cellulosum (Myxobacteria)
AUTHOR(S): Ahn, Jong-Woong; Lee, Chong-Ock
CORPORATE SOURCE: Division of Ocean Science, Korea Maritime University, Pusan, 606-791, S. Korea
SOURCE: Han'guk Misaengmul-Saengmyongkong Hakhoechi (2004), 32(1), 47-51
CODEN: HMHAAS; ISSN: 1598-642X
PUBLISHER: Korean Society for Microbiology and Biotechnology
DOCUMENT TYPE: Journal
LANGUAGE: Korean

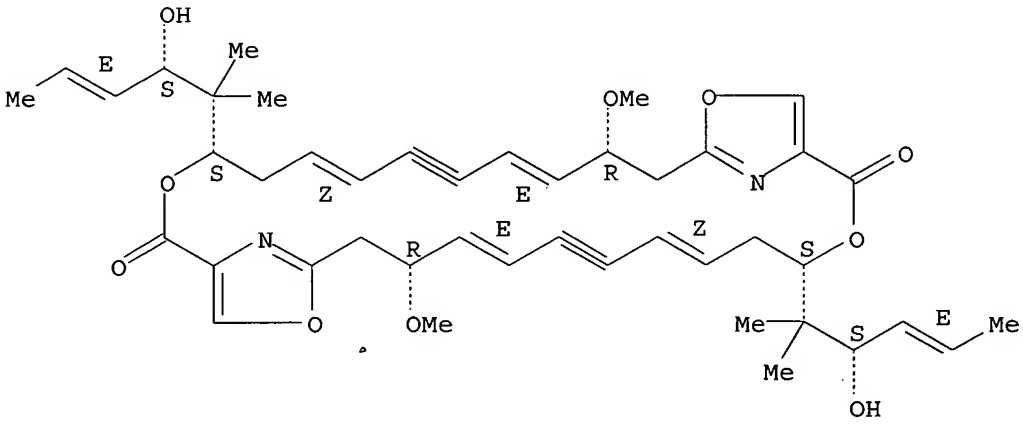
AB Drug resistance is one of the most significant impediments to successful chemotherapy of cancer. Multidrug-resistance is characterized by decreased cellular sensitivity to anticancer agents due to the overexpression of P-glycoprotein. By using adriamycin-resistance CL02 cancer cells, we undertook the screening for agents which were effective to multidrug-resistant cancer cells from strains of the species Sorangium cellulosum isolated in our laboratory Sorangium cellulosum, cellulose-degrading myxobacteria have recently proved to be a rich source of novel anticancer agents. One of the significant examples is the promising anticancer agent epothilone. JW1006 is the first strain of Sorangium cellulosum which was selected by us for the isolation of a metabolite by a biol. screening because of a high cytotoxic activity against the CL02 cancer cells. Cytotoxicity-guided chromatog. fractionation of the culture broth led to the isolation of two active principles, disorazole A1 and A2. They showed potent cytotoxicity against CL02 cancer cells with IC50 values in the picomolar range, and were as active against drug-resistant cancer cells

PAGE 1-B

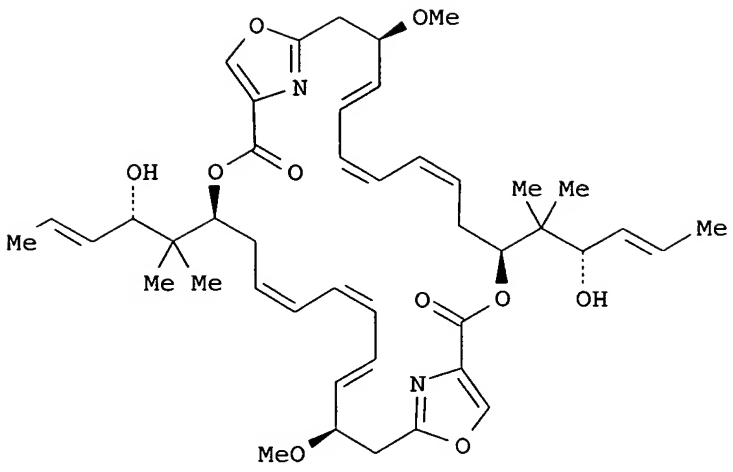


RN 809285-88-9 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,10,14(34),16,22,26,30(33),32-octaene-8,24-diyne-2,18-dione, 4,20-bis[(2S,3E)-2-hydroxy-1,1-dimethyl-3-pentenyl]-12,28-dimethoxy-, (4S,6Z,10E,12R,20S,22Z,26E,28R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as described by E or Z.



IT **158181-52-3P**, Disorazole C1
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-disorazole C1)
RN 158181-52-3 CAPLUS
CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-



I

AB The antimitotic natural product disorazole C1 (I) was isolated in 1994 from the fermentation broth of the myxobacterium Sorangium cellulosum. The authors have developed a highly convergent and stereoselective total synthesis of this compound which establishes its relative and absolute configuration. Key features of our synthesis include a highly convergent strategy and selective functional group manipulations that minimize decomposition of the sensitive polyene macrodiolide.

IT **809285-62-9P 809285-88-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (-)-disorazole C1)

RN 809285-62-9 CAPLUS

CN 3,15,19,31-Tetraoxa-33,34-diazatricyclo[28.2.1.114,17]tetratriaconta-6,10,14(34),16,22,26,30(33),32-octaene-8,24-diyne-2,18-dione, 12,28-dimethoxy-4,20-bis[(2S,3E)-2-[(4-methoxyphenyl)methoxy]-1,1-dimethyl-3-pentenyl]-, (4S,6Z,10E,12R,20S,22Z,26E,28R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as described by E or Z.

PAGE 1-A